

NMR OF HIGHLY FLUORINATED MOLECULES

By

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The NMR spectra of several chlorofluorocarbon and fluoro-ether molecules were assigned and characterized using one- and two-dimensional spectroscopy. The fluorine chemical shifts in chlorinated fluorocarbon molecules were described with additivity rules developed in this laboratory. Homonuclear correlation peaks among several inequivalent geminal fluorine nuclei showed different intensities. The different intensities for these correlation peaks were used to assign inequivalent geminal nuclei that are likely to participate in separate "through-space" spin-spin coupling pathways between adjacent vicinal fluorines.

Carbon-13 spectra, both coupled and fully decoupled from their fluorine ligands, are presented. Heteronuclear multiple quantum coherence spectra correlated the carbon-13 resonances with their fluorine ligands. The carbon-fluorine coupling constants for these molecules were tabulated, and their trends were discussed. A theoretical interpretation for an unusually large two-bond carbon fluorine coupling constant, offered collaborators, is discussed.

CHAPTER 1

INTRODUCTION

Fluorine-19 is a nucleus that is very receptive to study with nuclear magnetic resonance. Like hydrogen, it has a nuclear spin angular momentum number of 1/2, it is very abundant in nature, and has a large nuclear magnetic moment. Because of these similarities to proton NMR, some of the strategies developed for hydrogenated molecules can be applied directly to the NMR of perfluorinated molecules. However the NMR spectroscopy of highly fluorinated molecules differs from the spectroscopy of hydrogenated molecules in several ways:

1. Fluorine nuclei have a large chemical shift dispersion.
2. Long range nuclear spin-spin coupling is common for perfluorinated molecules.
3. The spin-rotation interaction is a significant relaxation mechanism in perfluorinated molecules.

The differences between the two classes of compounds limit the manner in which one can transfer NMR methods developed for hydrogenated molecules to study highly fluorinated ones. We will briefly review the origin of these differences before presenting the details of this investigation into the nature of highly fluorinated molecules.

Both the chemical shift interaction and the indirect nuclear coupling are anisotropic interactions that are represented by second rank tensors. However, molecules in a liquid medium are rapidly tumbling so the anisotropic components of the second rank tensor are averaged to zero. This study is concerned only with liquids, so we report the chemical shift and coupling constants, i.e., $(1/3)\text{Tr}[s]$ and $(1/3)\text{Tr}[J]$.

Both the chemical shift constant and the spin-spin coupling constant depend upon interactions between the nucleus and the electrons in the molecule. The spin-rotation interaction is associated with the change in angular momentum of the molecule.

Chemical Shift

The distinct absorption frequencies of the nuclei that we observe in the NMR spectrum are a result of the different local magnetic fields. Electrons have an energy due to a coupling of their angular momenta to the static magnetic field. The external magnetic field induces a motion of electrons such that a secondary local magnetic field is produced and alters the effective field at the site of the nucleus. Following the model due to Ramsey,¹ the expression for the chemical shift is given by

$$\sigma_{\Lambda\alpha\beta} = \sigma_{\Lambda\alpha\beta}^d + \sigma_{\Lambda\alpha\beta}^p \quad (1.1)$$

where

$$\sigma_{\Lambda\alpha\beta}^d = \frac{\mu_0 e^2}{8\pi m} \langle \psi_0 | (r_i r_{i\Lambda} \delta_{\alpha\beta} - r_{i\alpha} r_{i\beta}) r_{i\Lambda}^{-3} | \psi_0 \rangle, \quad (1.2)$$

and

$$\sigma_{\Lambda\alpha\beta}^p = -\frac{\mu_0 e^2}{8\pi m} \sum_{k \neq 0} \frac{\langle \psi_0 | \sum_i L_{i\alpha} | \psi_k \rangle \langle \psi_k | \sum_i L_{i\beta} r_{i\Lambda}^{-3} | \psi_0 \rangle + \langle \psi_0 | \sum_i L_{i\alpha} r_{i\Lambda}^{-3} | \psi_k \rangle \langle \psi_k | \sum_i L_{i\beta} | \psi_0 \rangle}{E_k - E_0} \quad (1.3)$$

The subscripts α and β refer to the Cartesian components x , y , and z . The distance between electron i and nucleus A is denoted by $r_{i\Lambda}$. The electron orbital angular momentum is denoted by L_i . The Kronecker delta is denoted by $\delta_{\alpha\beta}$, and μ_0 is the permittivity of free space.

The term that depends solely on the spatial operators, σ^d , is called the diamagnetic part of the chemical shift. The terms that include both angular momentum and spatial operators are collectively called the paramagnetic term. The paramagnetic term is a consequence of various effects, including the tendency for other nuclei in the molecule to hinder the electronic current around a specific nucleus, an attribute of the chemical environment of the nucleus. The names diamagnetic and paramagnetic arise from their similarity to the Van Vleck formulation of the magnetic susceptibility tensor.

The spherically symmetric field of s electrons has zero angular momentum and there are no low-lying excited states available to these electrons. Consequently, the paramagnetic term vanishes for the hydrogen nuclei, accounting for their small chemical shift dispersion. On the other hand, the fluorine nucleus has excited states that are lower lying than hydrogen, and its ground state involves p orbitals. Thus perfluorinated molecules have a chemical shift dispersion that is at least 20 times larger than that of protons.

There are several factors that complicate calculating the chemical shift using molecular orbital theory. First, the paramagnetic term opposes the influence of the diamagnetic term. Both of these terms may grow with the size of the molecule; so the total chemical shift is the small difference between two large terms and this situation tends to produce a large uncertainty. Second, the distances, r , in the Ramsey model are referred to an arbitrary origin, so that the calculated value of S_{tab} often depends on the origin chosen for the calculation. This is commonly referred to as gauge dependence^{2,3}. Moreover, the electronic eigenfunctions for the ground and excited states are obtained in the absence of the magnetic fields. When an atom is placed in an electric field of another nucleus, its orbital angular momentum is quenched. The presence of a magnetic field will generally lower the energy for the paramagnetic electronic circulation. Nonetheless, the resulting zero-field functions are used to represent ground state electronic structure in the presence of a magnetic field.

It is not necessary to break the chemical shift into the two separate terms. Indeed Oddershede⁴ has shown some promising results that show that the Gauge dependence can be reduced if one combines both terms together. Nonetheless, programs that calculate the chemical shift constant using have had fair amount of success despite the difficulties in the Ramsey model

Only a few people report the absolute shielding value. The chemical shift value is usually reported relative to a standard compound. The standard compound most commonly used for fluorine NMR is trichlorofluoromethane whose chemical shift value is taken to be zero. Most fluorine nuclei in organic molecules are more shielded than this reference compound: They normally have a negative chemical shift.

Because of the difficulties in calculating the values of chemical shifts, they are principally used in an entirely empirical way for structure determination. Nonetheless, models have been developed where the chemical shift is composed of a number of local contributions.^{5,6} The local contributions permit the nuclear shielding to be discussed in terms of chemically interesting aspects of the molecule. One of these local contributions is the distribution of electron density near the nucleus of interest. Thus the chemical shift values are affected by factors that affect the local electron density.

Another such local factor is the intramolecular electric field created by certain substituents in a molecule. These fields affect the electron polarizability in the rest of the molecule and will therefore affect the screening constant. Wallace Brey has studied the way in which chlorine substituents affect the chemical shift values of perfluorinated molecules. He found that the substitution of a chlorine for fluorine on nearby carbon atoms can be represented by an additive scale in the following manner:

1. For each chlorine atom on a carbon alpha to the fluorine nucleus of interest, add 6 parts per million to its normal chemical shift.
2. For each chlorine atom located on a carbon beta to the fluorine nucleus of interest, add 3 parts per million to its normal chemical shift.

A chlorine atom on a carbon gamma to the fluorine nucleus of interest does not influence its chemical shift significantly.

It seems reasonable that the polarizable chlorine atoms may induce a Van der Waals type of interaction that affects chemical shielding in the fluorine nuclei on the alpha and beta carbons. Furthermore, the large chlorine atoms may distort bond angles and bond distances which in turn may contribute to the chlorine substituent effect on the fluorine chemical shift.

As is the case with other empirical rules for the chemical shift, the additive scale above is very valuable for determining the structure of chlorofluorocarbons and analyzing their NMR spectra. It should also be noted that measured chemical shift variations between closely related molecules may arise not only from a change in chemical structure but that they may also represent an average value over several conformations. Furthermore, solute-solvent interactions can affect the value of the chemical shift.

Spin-Spin Coupling

The isotropic nuclear spin-spin coupling constant, J , in equation 1.4 is directly proportional to the energy of interaction between the induced field at atom N' and the magnetic moment on atom N':

$$\mathcal{H}_J = J_{NN'} \mathbf{I}_N \cdot \mathbf{I}_{N'}. \quad (1.4)$$

This nuclear coupling was discovered independently by Hahn and Maxwell,⁷ and by Gutowsky et al.⁸ In 1952, Ramsey and Purcell⁹ formulated a successful theory for spin-spin coupling, and Ramsey's theoretical estimates¹⁰ accounted for the order of magnitude of the observed coupling constant. They proposed that the magnetic moment of nucleus N perturbs surrounding electrons that induces a magnetic field at atom N' via electrons near nucleus N' that generate a magnetic field interacting with the magnetic

moment of N' . In their formulation, the nuclear spin-spin coupling arises from three basic contributions:

1. the nuclear-spin electron-orbit term, SO
2. the nuclear-spin-dipole electron-spin-dipole term, SD, and
3. the Fermi contact term, FC.

In the following discussion, the subscript n in $\mathcal{H}_n$ and the superscript n in J^n , (where $n=1, 2$, and 3) both refer to the contributions to the spin-spin coupling enumerated above: SO, SD, and FC respectively.

Theoretical Background

$\mathcal{H}_J$ operates only on the nuclear spin variables. In order to obtain the magnitude of $J_{NN'}$ the Hamiltonian,

$$\mathcal{H} = \mathcal{H}_0 + \mathcal{H}_1 + \mathcal{H}_2 + \mathcal{H}_3 \quad (1.5)$$

must operate on the total wavefunction, $\Psi = \psi_{\text{el}} \psi_{\text{nuc}}$.

$$\mathcal{H}\Psi = (\mathcal{H}_0 + \mathcal{H}_1 + \mathcal{H}_2 + \mathcal{H}_3) \psi_{\text{el}} \psi_{\text{nuc}} = E\Psi \quad (1.6)$$

We do not know the function ψ_{el} , and the equation above obliges us to determine the electronic wavefunction belonging to the Hamiltonian. The wavefunction--and hence the energy--is derived by a second order perturbation approximate method.¹¹ The sum over states second order perturbation contribution to the energy is given by the following equation:

$$E_{1n}^{(2)} = \sum_{n \neq 0} \frac{\langle \Psi_0 | \mathcal{H}_1 | \Psi_n \rangle \langle \Psi_n | \mathcal{H}_1 | \Psi_0 \rangle}{(E_0 - E_n)} \quad (1.7)$$

Convergence for this expression can be slow. Moreover successive terms do not always diminish in magnitude. So extending the number of terms in the summation by using a configuration interaction can lead to results that are worse than results obtained by a minimal basis set.¹²

The Nuclear-Spin–Electron-Orbit term

The spin-orbit (SO) term arises from the interaction between the electron orbital angular momentum and the nuclear spin angular momentum. The Hamiltonian describing the energy of an electron moving in the magnetic field generated by a magnetic moment μ_A is

$$\mathcal{H} = \frac{1}{2} \sum_k \left(\frac{1}{i} \nabla_k + \frac{1}{c} \sum_N \gamma_N \frac{\mathbf{I} \times \mathbf{r}_{kN}}{r_{kN}^3} \right)^2 + V \quad (1.8)$$

where ∇_k is the spatial gradient operator for electron k , $\mathbf{r}_{kN}$ is the distance vector from the nucleus N to electron k , and V are the collective potential terms for pairs of electrons and nuclei. $\mathbf{I}$ is the nuclear spin angular momentum operator, and γ_N is the nuclear magnetogyric ratio. The Hamiltonian above breaks down into two separate terms, the diamagnetic spin-orbit term

$$\mathcal{H}_{1a} = \frac{e\hbar\beta}{c} \sum_{N,N'} \gamma_N \gamma_{N'} \sum_k \frac{(I_N \cdot I_{N'})(r_{kN} \cdot r_{kN'}) - (I_N \cdot r_{kN})(I_{N'} \cdot r_{kN'})}{r_{kN}^3 \cdot r_{kN'}^3}, \quad (1.9)$$

and the paramagnetic spin-orbit term

$$\mathcal{H}_{1b} = 2\beta\hbar \sum_N \gamma_N I_N \cdot \left(\sum_k \frac{\mathbf{L}_{kN}}{r_{kN}^3} \right). \quad (1.10)$$

The evaluation of the diamagnetic spin-orbit term requires a first order perturbation treatment, while the evaluations of the paramagnetic term require a second order perturbation treatment. The few authors who have calculated J^{1a} find that the contributions from different regions of space cancel, leading to a minuscule total contribution.¹³ However, Perera, at the University of Florida, has recently communicated to this author calculations that he performed on small hydrogenated molecules that suggest that this term could have an appreciable contribution to the total coupling constant.

As was suggested previously, the interaction leading to the spin-orbit term is anisotropic, so calculations for the paramagnetic term must be repeated for the nuclear moment in the x and y directions. The isotropic part of J^{1b} is then obtained as an average of J_{xx}^{1b} , J_{yy}^{1b} , J_{zz}^{1b} ,

$$J^{1b}(NN') = \frac{1}{3} [J^x(NN') + J^y(NN') + J^z(NN')]. \quad (1.11)$$

The Nuclear-Spin-Dipole Electron-Spin-Dipole Term

The Hamiltonian expressing the mutual potential energy between the magnetic moments of electron k and nucleus N is written as

$$\mathcal{H}_2 = 2\beta\hbar \sum_N \gamma_N \sum_k \left[\frac{3(S_k \cdot r_{kN})(I_N \cdot r_{kN})}{r_{kN}^5} - \frac{S_k \cdot I_N}{r_{kN}^3} \right]. \quad (1.12)$$

The electron-spin angular momentum operator is represented by S_k ; β is the Bohr magneton, and $\hbar$ is Planck's constant divided by 2π .

The form of the Hamiltonian makes the spin-dipolar term more complicated to handle than the other two second order terms. During the evaluation of $\mathcal{H}_2$, the operators S_x and S_y mix both α and β electron spins and introduce real and imaginary perturbations

to the wavefunction. Consequently, both the basis set and the self-consistent field procedures above must be modified so that all the matrices representing the one- and two-electron operators can be partitioned. As for the spin-orbit term, the anisotropic components for the spin-dipolar (SD) term are collected and expressed as an average.

$$J^2(\text{NN}') = \frac{1}{3} [J^{xx} + J^{yy} + J^{zz} + 2(J^{xy} + J^{xz} + J^{yz})] \quad (1.13)$$

Note that the off-diagonal terms are more heavily weighted.

The Fermi Contact Term

When the electron and nucleus are in contact, r_{KN} is zero, and the spin-dipolar Hamiltonian leads to a catastrophe.¹⁴ Of course s electrons have a nonzero probability for being at the nucleus and the Fermi contact (FC) term attempts to account for this probability. Enrico Fermi¹⁵ first considered this problem in the hyperfine interaction of the hydrogen atom when he developed the Hamiltonian that bears his name:

$$\mathcal{H}_3 = \frac{16}{3} \pi \beta \hbar \sum_N \gamma_N \sum_{\mathbf{k}} \delta(r_{\text{KN}}) \mathbf{S} \cdot \mathbf{I}_N \quad (1.14)$$

The Dirac delta function, $\delta(r_{\text{KN}})$, is nonzero only where r_{KN} is zero.

Like the other two paramagnetic terms, the Fermi contact term requires a second order perturbation treatment. In contrast to the other contributions to the coupling tensor, the Fermi contact contribution is isotropic. Moreover the nonzero diagonal elements are equal. This term is nearly always the dominant contribution to the magnitude of $J_{\text{NN}'}$ when hydrogen couples with a second row element. Often times it is large for the coupling between a fluorine atom with another second period element, but it may not necessarily be the largest contribution to the coupling constant in this instance. Indeed the contributions of the spin-orbit and spin-dipolar terms to fluorine-fluorine coupling are appreciable.^{16,17}

Trends in Fluorine-Fluorine J coupling

The four- and five-bond spin-spin coupling constant between two fluorine nuclei ($^4J_{FF}$ and $^5J_{FF}$) is often larger than the three-bond fluorine spin-spin coupling constant, $^3J_{FF}$. This is unlike the hydrogen coupling constant, which decreases monotonically with the increase in the number of bonds between the two protons of interest. Saika and Gutowsky¹⁸ suggested that the coupling has two or more contributions described above that are of comparable magnitude, and with opposing signs, that attenuate at different rates with the number of intervening bonds.

The coupling constant between two fluorine nuclei is greatly dependent on substituent electronegativity. Indeed several authors have shown that a linear relationship exists between the magnitude of the average coupling constant and the sum of the electronegativities of the other substituents on the carbon atoms.^{19,20} Figure 1-1 and Table 1-1 serve to illustrate this phenomenon. When the substituents W, X, Y, and Z are all fluorines, $^3J_{FF}$ is a small negative value.

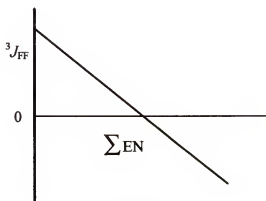


Figure 1-1

Magnitude of $^3J_{FF}$ versus the sum of the electronegativity of the vicinal substituents

Table 1-1

W	X	Y	Z	$^3J_{FF}$
F	F	F	F	$-1 < J < 0$
Cl	F	F	F	$0 < J < 1$
Cl	Br	F	F	$0 < J < 1$
Cl	Br	C	F	$J < 1$
Cl	Br	C	N	observable

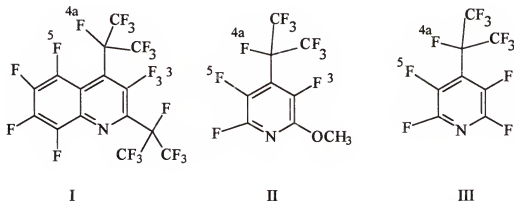
Hirao and co-workers^{21,22} calculated values of $^3J_{FF}$ for saturated fluorocarbons that suggest that the substituent effects on $^3J_{FF}$ dominate over its dependence on the dihedral angle. The situation is a bit more ambiguous for the four-bond coupling constant: some investigators believe that $^4J_{FF}$ could have a stereochemical dependence.^{23,24,25,26}

Through-Space Coupling

In certain instances, anomalously large coupling constants are observed for nuclei that are many bonds apart but physically close in space.^{27,28} This occurs most frequently for fluorine-fluorine nuclear coupling, but can also occur with other nuclei. The term 'through-space' is meant to imply that the intervening bonds between the two coupled nuclei play a less significant role than one finds in ordinary indirect nuclear coupling. Electrons are thought to transmit the nuclear coupling information through the overlap of nonbonding or antibonding orbitals.²⁹ The normal route for the coupling information is through bonds and the overlap of bonding orbitals; so the through-space mechanism is a sort of molecular short circuit. Several investigators attribute the through-space mechanism to a Fermi contact interaction.^{30,31}

There has been some speculation as to whether the sign of the coupling constant is an indication of the through space mechanism. Wasylishen and Schaefer³² used an INDO

theory to study the coupling in methyl substituted benzenes. In conformations of ortho xylene where the coupled methyl protons are in close proximity, they predicted that there would be negative through-space coupling. Chambers et al.³³ measured the signs of the through-space coupling in several perfluorinated aromatic compounds: 1,4-perfluoro-isopropyl-perfluoronaphthalene (I), 1-methoxy-4-perfluoro-isopropylpyridine (II), and 4-perfluoro-isopropyl-pyridine (III). They found the coupling constant between the 4a fluorine nucleus of the perfluoropropyl chain in each molecule and the aromatic fluorine nucleus, 5 or 3, in close proximity to 4a, is positive. Manatt and coworkers³⁴ report that the sign of the 1,8 coupling between two fluorine nuclei in difluoronaphthalene is positive.



Myhre et al.³⁵ studied the through-space coupling in several alkylfluorobenzenes. They introduced substituents to the ring to induce conformational changes in the alkylfluoro substituents. Using the results of their conformational analyses, they plotted the $^5J_{\text{HF}}$ against the internuclear distance. While they did not fit their data to a specific function, their plot takes on an exponential appearance. Hilton and Sutcliffe³⁶ used data from the work of Gutowsky and Mochel³⁷ and data from Chambers and coworkers³⁴ to make a plot of the fluorine through-space coupling. They found that the through-space coupling decreases exponentially as the distance between the two coupled fluorine nuclei

increases. The exponential decay of the magnitude of the through-space coupling with increasing interatomic distance was confirmed by Ruiz de Azua et al.³⁸

The work of Myhre et al.³⁶ and the research of Servis and Fang³⁹ suggested that the through-space coupling between two fluorine nuclei is insensitive to changes in electron density within the aromatic ring. Later Mallory and coworkers confirmed this observation in their examinations of substituted naphthalene and phenanthrene systems.⁴⁰ Indeed their examination of the through-space coupling between the fluorine nuclei at the number one and twelve positions in the benzo[c]phenanthrene system demonstrates that this insensitivity to electronic effects is characteristic of the through-space coupling that operates in both nonplanar and planar geometries.

A number of years ago, several investigators suggested that the through-space mechanism for indirect nuclear coupling was the dominant mode of transmission in fluorine molecules⁴¹. We know today that this is not always the case. Nonetheless there can be no doubt that a through-space mechanism is important for the transmission of spin-spin coupling information in perfluorinated molecules.

The Spin-Rotation Relaxation

At room temperatures the spin-lattice relaxation rates for fluorine nuclei are usually larger than those of protons, and, for some molecules at some temperature range, the spin-lattice relaxation rate for fluorine increases with increasing temperature. This temperature dependence is unique to the spin-rotation relaxation mechanism: The other relaxation mechanisms have the opposite temperature dependence.

Table 1-2 is reproduced from Watkins⁴². It illustrates the temperature dependence of the two contributions to the total spin-lattice relaxation time of p-chlorofluorobenzene. The spin-lattice relaxation time is decomposed into its intermolecular and intramolecular contributions. The spin-rotation

and dipolar interaction both contribute to the intramolecular spin-lattice relaxation rate, but only the dipolar interaction contributes to the intermolecular relaxation rate.

The spin-rotation relaxation mechanism arises from the coupling of changes in magnetic field associated with changes in molecular angular momentum and the nuclear

Table 1-2

Temp (°C)	T _{1 intra} (sec)	T _{1 inter} (sec)	T _{1 sr} (sec)	T _{1 intra d} (sec)
100	19.7	-	34	46.8
90	20.7	-	41	41.7
80	21.5	-	51	36.6
70	22.8	98.0	66	34.2
60	24.0	80.8	81	34.2
50	25.2	65.5	102	33.3
40	25.5	57.8	135	31.4
30	25.2	52.3	177	29.8
20	24.0	49.8	350	25.5
10	23.1	43.8	-	23.1
0	22.2	35.7	-	22.2
-10	20.7	29.1	-	20.7
-20	19.1	24.3	-	19.1
-30	16.6	21.2	-	16.6

magnetic moments. Two models exist that explain the temperature dependence of the spin-rotation interaction. In a model proposed by Hubbard,⁴³ the angular velocity of the molecule is treated classically by assuming that the molecule has a rotational diffusion constant. The change in molecular orientation is proposed to be due to isotropic rotational Brownian motion. The treatment for the conditional probability density for the angular velocity in rotational Brownian motion is analogous to the treatment used to describe translational Brownian motion. Molecular collisions due to Brownian motion interrupt the coupling of angular momenta between the molecule and the nucleus and induce a relaxation mechanism where the nuclear spin energy is transferred directly to the process of molecular rotation.

A correlation function for the rotational motion is formulated for an exponentially decaying correlation, with a time constant t_{sr} . This correlation time between molecular collisions, t_{sr} , is much smaller than the correlation time for molecular reorientation, t_c . Moreover t_{sr} decreases with increasing temperature while t_c increases with temperature. The relationship between the two correlation times is given by the Hubbard equation

$$\tau_c \tau_{sr} = I_r / 6kT. \quad (1.15)$$

In the above expression I_r is the molecular moment of inertia, k is the Boltzman constant, and T is the absolute temperature.

The nuclear spin-rotation relaxation rate in this model is given by

$$T_{1sr}^{-1} = \left(2I_r kT \tau_{sr} / 3\hbar^2 \right) (2C_{\perp}^2 + C_{\parallel}^2). \quad (1.16)$$

where $\hbar$ is Planck's constant in angular units, and $C_{\perp}$ and $C_{\parallel}$ are the perpendicular and parallel components of the spin-rotation interaction tensor. For a spherical molecule in an isotropic medium, these tensor components can be replaced with the spin-rotation interaction constant, C .

An alternative model was proposed by Brown and co-workers⁴⁴. They recognized that the statistical properties of the spin-rotational interaction in a liquid may be different from those of the orientation-dependent interactions. For their model, the orientation of the molecule and its angular momentum are completely uncorrelated. This enabled them to propose that the molecules jump from one orientation to another at random times. The spin-rotational interaction is assumed to operate during these jumps when the molecule is actually rotating and the magnetic field produced from the molecule is zero except for this momentary pulse. They consider that the molecule is restrained from rotating through its

interaction with a cage of other molecules. Reorientation occurs where the cage expands or when the molecule acquires enough energy to overcome the potential barrier.

The transient rotation model leads to the following expression for the spin-rotational contribution to the spin-lattice relaxation time:

$$1/T_1 = (1/3) \left(\gamma^2 \langle H_{sr}^2 \rangle_{Av} \Delta^2 / \tau_{sr} \right) \quad (1.17)$$

In this expression $\langle H_{sr}^2 \rangle_{Av}$ is the mean-squared magnitude of the magnetic field generated at the fluorine nucleus during a reorientation and Δ is a time between random events that is much shorter than τ_{sr} . If $\Delta = \tau_{sr}$, the transient rotation model is identical to a model proposed by Johnson and Waugh⁴⁵ to describe the spin-rotation interaction of H₂ gas. Now Δ is the time elapsed between events that change a molecule from one discrete rotational state to another. When comparing their model for liquids to that of Johnson and Waugh for gases, Brown et al. described the fraction by which Δ is less than τ_{sr} as the quenching of molecular rotation and the spin-rotational interaction in the liquid state.

The dipole-dipole relaxation mechanism is more common to spin 1/2 nuclei than is relaxation via spin-rotation. Relaxation via the dipole-dipole mechanism is responsible for a valuable tool, called the nuclear Overhauser effect (NOE),⁴⁶ that can be used to determine spatial relationships within a molecule. The spin-rotation mechanism is usually expected to be important for small molecules and for short aliphatic side chains that rotate rapidly at high temperatures. When the spin-rotation relaxation mechanism is effective, it competes with the dipole-dipole relaxation mechanism. This could have deleterious effects for the nuclear Overhauser effect (NOE). So, unlike for protonated molecules, it is difficult to determine various conformations in perfluorinated molecules with NMR.

CHAPTER 2 HOMONUCLEAR FLUORINE CORRELATION SPECTROSCOPY

Overview of Correlation Spectroscopy

Before 1982, one type of double resonance experiments, called selective decoupling, was an extremely popular method for simplifying NMR spectra. These experiments are a straightforward approach to removing scalar interactions in the spectrum. However, the limitations of these experiments are reached quickly. Double irradiations become nonselective when multiplets in the spectrum are not well resolved from one another. Nonresolved multiplets are common to the NMR spectrum of fluorocarbons with more than a five-carbon atom backbone, and also common in proton NMR when the molecule increases in size and complexity. In these situations, a single irradiation could result in a maze of decoupling pathways that may not be disentangled. Moreover, this technique is cumbersome when numerous decouplings are needed.

The results from a systematic series of double resonance experiments suggested a correlation diagram. Rather than placing these results inside the diagram, Jeener⁴⁷ suggested measuring the response of the scalar coupling pairwise interaction to a two-pulse sequence that is Fourier-transformed with respect to both time variables. Five years after Jeener conceived the two-dimensional correlation experiment, a group working in Ernst's laboratory brought his idea into practice.⁴⁸ Since that time, the development of multi-dimensional spectroscopy went on to where more than 500 pulse sequences are available for use. Nevertheless, the original Jeener experiment remains the workhorse, and as in the spectroscopy of large organic and biomolecules, the Jeener experiment is indispensable to the spectroscopy of perfluorinated molecules.

Correlated Spectroscopy, or COSY, not only is more convenient and faster than selective decoupling experiments, but it also removes the need to make assignments based on assumptions such as that a fluorine nucleus near a nitrogen should be at lower field than one near a chlorine atom. In proton spectroscopy, there may exist favorable conditions in the two-dimensional COSY spectrum where one may detect cross peaks due to couplings that are less than the observed linewidth in the one-dimensional spectrum. In principle there are more opportunities for one to observe this situation in the fluorine two-dimensional spectrum because there are many more lines where the scalar nuclear coupling is unresolved. However the best opportunity to resolve these couplings in the case of fluorine NMR may result from especially designed selective one-dimensional versions of the two-dimensional experiment⁴⁹ because success depends upon high digital resolution.

If the value of the coupling constant is not required, it is not necessary to have high digital resolution to establish the connectivities of the molecule through its indirect nuclear coupling. Since two chemical shifts contribute to the position of a cross-peak, there is a lower probability of accidental overlap. Furthermore, the fluorine chemical shift dispersion for the molecules in this study is about eight times wider than that of proton NMR; consequently, one can learn something even with low digital resolution.

All the coupling pathways are probed simultaneously. Beginning from a suitable starting point, one traces the couplings via the off-diagonal peaks to establish the connections between the atoms in the molecule. For proton NMR, knowing that one coupling constant is 7 Hz and another is 3 Hz can help one establish that the larger coupling constant is vicinal and that the smaller one is four bonds away, but the magnitudes of the fluorine coupling constants reveal this information differently. The vicinal fluorine-fluorine coupling constant in highly fluorinated molecules is usually near zero, and only the two-bond, four-bond and longer range couplings are available to us. Thus the coupling network in the fluorine two-dimensional homonuclear correlation spectrum reveals a correlation map that typically looks as follows:



On the other hand, the proton correlation spectrum would reveal a different type of map.



A wide chemical shift dispersion is a disadvantage as well as a blessing because fluorine two-dimensional spectra require even more time and much more computer disk space than does a better resolved proton two-dimensional spectrum. Moreover, without a specially constructed probe, it is difficult to excite the fluorine spectrum evenly. A consequence of an uneven excitation for two-dimensional spectroscopy is a phase variation across the spectrum. It is difficult to measure the coupling constant for peaks with poor phase. Also poor phase makes it difficult to distinguish a passive from an active coupling.

Dynamics of Homonuclear Correlation

Spectroscopists normally decompose a two-dimensional NMR experiment into four periods of time: a preparation period, an evolution period (t_1), an optional mixing period, and a detection period (t_2). In the preparation period the spin system is usually prepared in a coherent nonequilibrium state that will evolve in the following segment, the evolution period. The evolution time, t_1 , is incremented stepwise and determines the frequencies in the ω_1 domain. For each t_1 increment, we detect a separate free induction decay (FID) in t_2 . Large numbers of increments in the acquisition of the t_1 dimension ensure that it is well resolved, just as long acquisition times during t_2 ensure that this

dimension is well resolved. During the mixing period, single-, multiple-, or zero-quantum coherence is transformed into observable transverse magnetization.

The multi-dimensional NMR spectrum is a representation of the transfer process of coherence, where peaks arise at the characteristic frequencies, Ω , of each of the interconnected coherences. Coherence is a generalization of magnetization and is formally represented in the off-diagonal elements of the density matrix,⁵⁰ $\rho = |\Psi(t)\rangle\langle\Psi'(t)|$. If Ψ is an eigenstate for the system, it has no off-diagonal elements in ρ . This is an example of a pure state. In a real system we are concerned with an ensemble of spins in a mixed state; so we can only indicate the probabilities p^k that a spin system of the ensemble is in the k th state. In a coherent superposition of eigenstates, the time dependencies and phases of the various states in an ensemble are correlated with the time dependencies and phases of other states. The coherence is preserved during the evolution of the chemical shift.

The effect of using a pulse to rotate the $|\alpha\rangle$ state into the $|\beta\rangle$ state establishes a coherence between the two states across a single nuclear transition. Although there may exist coherences of various orders associated with the transitions of many combinations of energy levels, we only directly detect single-quantum coherence allowed by the selection rule $\Delta m_z = \pm 1$. These detectable single-quantum coherence levels are represented by a single transverse operator, I_x or I_y . There also may exist antiphase coherence terms such as $2I_{1y}I_{2z}$ that are not directly observed, but they can be converted into an observable magnetization. Indeed this very situation occurs during the COSY experiment. A shorthand notation was developed to express the description above.⁵¹ We represent a pulse of flip angle β with a phase angle ϕ by the rotation operator β_ϕ . For example,

$$I_z \xrightarrow{\beta_x} I_z \cos \beta - I_y \sin \beta. \quad (2.1)$$

The chemical shift precession is denoted by $\Omega I_z t$. The shorthand description proceeds in the following manner:

$$I_y \xrightarrow{\Omega I_z t} I_y \cos \Omega t - I_x \sin \Omega t \quad (2.2)$$

The coherent effects of the indirect coupling introduce one or more new operators into description of the system. Following the shorthand convention, we represent the effects of indirect coupling during evolution for a period t as a product of spin operators, with the two nuclei labeled 1 and 2:

$$I_{1x} \xrightarrow{2\pi J_{12} I_{1z} I_{2z}} 2I_{1x} \cos \pi J_{12} t + 2I_{1y} \sin \pi J_{12} t \quad (2.3)$$

$$2I_{1x} I_{2z} \xrightarrow{2\pi J_{12} I_{1z} I_{2z}} 2I_{1x} I_{2z} \cos \pi J_{12} t + 2I_{1y} \sin \pi J_{12} t \quad (2.4)$$

The AX system of two coupled spins permits us to illustrate the spin dynamics of the COSY spectrum. We shall note the evolution of the spin density operator at the periods marked 0, 1, 2, 3 in Figure 2-1.

Until point 0, the density operator, σ_0 , is composed of the two spins at equilibrium:

$$\sigma_0 = I_{1z} + I_{2z} \quad (2.5)$$

After the first $(\pi/2)_x$ pulse, the density operator σ_1 is composed of transverse spin operators, as in Eq. 2.1:

$$\sigma_1 = - (I_{1y} + I_{2y}) \sin \pi/2 \quad (2.6)$$

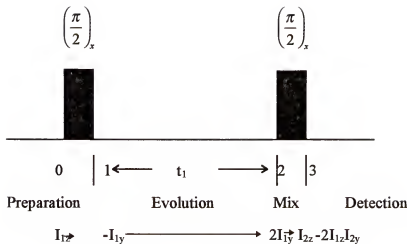


Figure 2-1
COSY Pulse Sequence

During the evolution period, the chemical shift interaction labels the transverse operators with their respective precession frequencies and the indirect nuclear coupling creates products of spin operators in an antiphase state. The density operator at point 2 is transformed into

$$\begin{aligned} \sigma_2 = & [-I_{1y}\cos \Omega_1 t_1 + I_{1x}\sin \Omega_1 t_1 - I_{2y}\cos \Omega_2 t_1 + I_{2x}\sin \Omega_2 t_1]\cos(\pi J_{12} t_1) + \quad (2.7) \\ & [2I_{1x}I_{2z}\cos \Omega_1 t_1 + 2I_{1y}I_{2z}\sin \Omega_1 t_1 + 2I_{2x}I_{1z}\cos \Omega_2 t_1 + 2I_{2y}I_{1z}\sin \Omega_2 t_1]\sin(\pi J_{12} t_1) \end{aligned}$$

By means of a second $\pi/2$ pulse with phase x , it is possible to transfer the coherence of spin 1 which is antiphase with respect to spin 2, represented by $2I_{1y}I_{2z}$, into the coherence of spin 2 antiphase with respect to spin 1, which is represented by $-2I_{1z}I_{2y}$. The earlier coherence of spin 1 has evolved with the chemical shift of nucleus 1 during t_1 and then is transferred by this pulse into coherence of spin 2 that evolves with its chemical shift frequency. The density operator at point 3, σ_3 , contains the product operators that are the basis of coherence transfer in correlation experiments:

$$\begin{aligned} \sigma_3 = & [I_{1x}\sin\Omega_1t_1 - I_{1z}\cos\Omega_1t_1 + I_{2x}\sin\Omega_2t_1 - I_{2z}\cos\Omega_2t_1]\cos(\pi J_{12}t_1) \\ & - [2I_{1x}I_{2y}\cos\Omega_1t_1 + 2I_{1z}I_{2y}\sin\Omega_1t_1 + 2I_{2x}I_{1y}\sin\Omega_2t_1 + 2I_{2z}I_{1y}\sin\Omega_2t_1]\sin(\pi J_{12}t_1) \end{aligned} \quad (2.8)$$

The new antiphase term $-2I_{1z}I_{2y}$ evolves into a detectable single transverse operator during acquisition under the influence of the chemical shift. Many more terms are generated for the pulse sequence above, but we only need to consider those terms that are relevant to the observable from a $\pi/2$ mixing pulse. The expectation value of an observable operator $\hat{I}$ in Liouville space is determined by calculating the trace of the product of the observable operator and the density matrix, $\hat{\sigma}(t)$,

$$\langle \hat{I} \rangle = \text{tr} \left\{ \hat{I}^\dagger \hat{\sigma}(t) \right\}. \quad (2.9)$$

The intensity of the crosspeak is determined by the coefficients in front of the product operators during the detection period.

COSY-45

Shortening the duration of the mixing pulse to $\pi/4$ allows one to examine the relative signs of the coupling constants.⁵² The relative signs revealed by the peak amplitudes are determined by the topology of the energy level diagram. We designate an active coupling as a coupling involved with the coherence transfer and responsible for the correlation cross-peak. A passive coupling partner will further split the crosspeak but does not transfer coherence via antiphase magnetization. However, the presence of a passive coupling partner is prerequisite for observing the relative signs of the coupling constants.

Transitions among the same active spins that do not share an intermediate energy level are described as parallel, while transitions between pairs connected by an

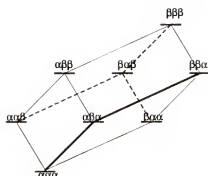
intermediate energy level are designated as progressive or regressive. In a progressive transition, the originating energy level and the final energy level are extrema in an energy level diagram. For a regressive transition, the intermediate energy level is the extremum. It is convenient to use polarization operators^{53,54} to describe the individual transitions in this relationship. For weakly coupled systems, polarization operators can be converted to the Cartesian product operators used to describe the effect of radio frequency pulses above. If the polarization relations between the two active nuclei, M and X, are opposite, $I_A^\alpha I_M^\beta I_X^\beta$ and $I_A^\alpha I_M^\alpha I_X^\beta$, then the transitions are said to be progressive. Active coupling partners whose polarization relations are the same, $I_A^\alpha I_M^\alpha I_X^\beta$ and $I_A^\beta I_M^\beta I_X^\beta$, are regressively connected. Progressive transitions lead to positive cross-peaks and regressive transitions result in negative cross-peaks in a phase-sensitive detection mode. It is useful to extend the relationship between directly connected energy levels to energy levels that are remote from each other--separated by a number of passive coupling partners--but bear the same progressive and regressive relationship between the active partners as the directly connected levels. As shown in Figure 2-2, the progressive transition among nuclei M and X above is direct since the polarization of the passive spin A was not inverted. On the other hand, the regressive transition is regressive to order 1 because the polarization of the single passive spin was inverted. Thus transitions are remotely progressive or regressive to order q if they can be made to share a common eigenstate in a progressive or regressive arrangement by inverting the polarizations of q passive nuclei.

We are not interested in calculating the amplitude of the individual transitions, but only in the qualitative description of crosspeaks in the spectra. If a resonance has coupling to q passive nuclei, then the crosspeak will be a superposition of q subspectral squares that arise from polarizations of the passive spins. When the mixing pulse is $\pi/4$, coherence transfer is restricted largely to directly connected transitions. The remotely connected transitions are not eliminated, but reduced. The resulting crosspeak obtains a skew relative to the diagonal. If the couplings to the passive spin J_{AM} and J_{MX} have the same

(a)

$$\begin{pmatrix} I_A^\alpha I_M^+ I_X^\beta \\ I_A^\alpha I_M^+ I_X^\alpha \end{pmatrix}$$

progressive transitions
q=0



(b)

$$\begin{pmatrix} I_A^\alpha I_M^+ I_X^\beta \\ I_A^\alpha I_M^\beta I_X^\alpha \end{pmatrix}$$

regressive transitions
q=1

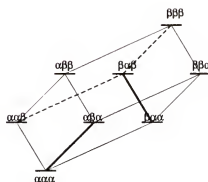


Figure 2-2

The parameter q classifies the order of connectivity between the two transitions under examination. The connectivity between either a progressive or a regressive pair of transitions is to order q , where q represents number of passive spins that must be inverted to obtain a configuration with one common eigenstate. (a) Direct progressive transitions in a three spin system. (b) Remote regressive transitions to order one.

sign, the line connecting the centers of gravity of the two squares subtends an angle $0 < |\phi| < \pi/4$ with respect to the diagonal. For $J_{AM} \times J_{MX} < 0$, this angle is $\pi/4 < |\phi| < 3\pi/4$.

These slopes allow us to determine the relative signs of the coupling constants in a manner analogous to the one-dimensional spin-tickling experiment where one type of transition--either progressive or regressive--is selectively irradiated. Interrogating the relative signs of all the coupling system at once is an advantage. However, in complicated systems the signs for some of the coupling partners may still remain ambiguous.

Double-Quantum Filtering

Groups of nuclei with spin $1/2$ may give rise to coherence levels greater than one if they are indirectly coupled via the electrons. NMR spectroscopists commonly use the double-quantum coherence level to reduce the signals from singlets and to reduce much of the dispersive character in the diagonal peaks. The pulse sequence is shown in Figure 2-3.

Multiple-quantum coherence is converted into observable coherence by placing a $\pi/2$ pulse after the normal COSY sequence. By using a suitable phase cycle, we select the double-quantum coherence from amongst a number of possible coherence levels. Part of the phase cycle is represented by the subscript in the first pulse, but one can also cycle the

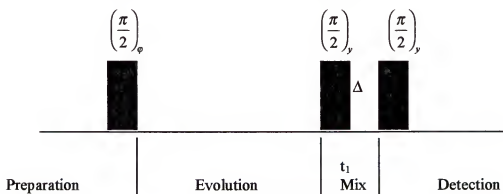


Figure 2-3
DQFCOSY Pulse Sequence

phase of the last pulse and obtain equivalent results. The fixed delay Δ is usually a few microseconds long and is there to allow the spectrometer to perform the requisite phase shift in going from the second to the third pulse.

We shall discuss the creation of double-quantum coherence in this sequence with the two $\pi/2$ mixing pulses along the y axis. A $2I_{1y}I_{2z}$ term is created by the first of two mixing pulses, and it is converted into a superposition of zero- and double-quantum coherence.

$$2I_{1y}I_{2z} \xrightarrow{\left(\frac{\pi}{2}\right)_y} 2I_{1y}I_{2x} = \frac{1}{2i} \left(I_1^+ I_2^+ - I_1^- I_2^- + I_1^+ I_2^- - I_1^- I_2^+ \right) \quad (2.10)$$

The zero-quantum terms are eliminated by cycling the phase of the first pulse, leaving only the double-quantum terms

$$\frac{1}{2i} (I_1^+ I_2^+ - I_1^- I_2^-) = \frac{1}{2} (2I_{1x}I_{2y} + 2I_{1y}I_{2x}). \quad (2.11)$$

The second $\pi/2$ mixing pulse with phase y converts this into $-\frac{1}{2} (2I_{1x}I_{2y} + 2I_{1y}I_{2x})$.

The second term, $2I_{1y}I_{2z}$, has been regenerated; so coherence is not transferred between coupling partners. In the first term, $2I_{1x}I_{2y}$, the coherence of spin 2 is transferred into the coherence of spin 1. The coherence transfer gives rise to a cross-peak between spin 1 and spin 2, and the regenerated term contributes to the diagonal peak. There is a loss in sensitivity associated with the double-quantum filter, but this is compensated by the reduction of the dispersion components in the diagonal peaks and of the t_1 noise associated with singlets.

Experimental

COSY spectra were taken at 7 tesla on a General Electric NT-300 and at 11 Tesla on a Varian Unity-500. Double-quantum filtered COSY (DQF-COSY) and COSY-45 spectra were recorded on the Unity-500. The fluorine transmitter frequency is 285 MHz for a 7 Tesla spectrometer and 470 MHz for an 11 Tesla system. The two-dimensional spectra collected on the NT-300 were collected in magnitude mode. COSY-45 spectra were also collected in magnitude mode, and the DQF-COSY were collected in the phase sensitive mode. In some of the COSY-45 spectra, a $\pi/4$ flip angle was unintentionally used also for the preparation pulse. This reduces the overall sensitivity of the spectra; however, sensitivity was not a problem for the molecules studied with this method.

The fluorocarbon samples were synthesized at the Wright-Patterson Air Force Base and then sent to this laboratory for spectral analysis after purification.

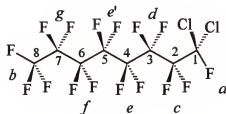
Results

In this section we examine and compare the spectra of chlorofluorocarbons and the spectra of fluoro-ethers. We will also use the correlation spectrum to analyze two mixtures of fluorocarbon compounds. We shall number positions in each molecule and place an alphabetic label on the individual spectral resonances as they appear from low to high field. As we discuss these spectra, the resonances, represented by the alphabetic labels, will be assigned to the chemical shift of a group of isochronous nuclei at a numbered position. The chemical shifts of nuclei that yield AB patterns⁵⁵ correspond to the geometric mean for the two peaks in each half of the pattern.

Spectra of Chlorofluoro-Alkanes

1,1-Dichloroperfluoro-octane (IV). In Figure 2-4 is the one-dimensional fluorine spectrum for this molecule. The complex fine structure of the resonances in this spectrum

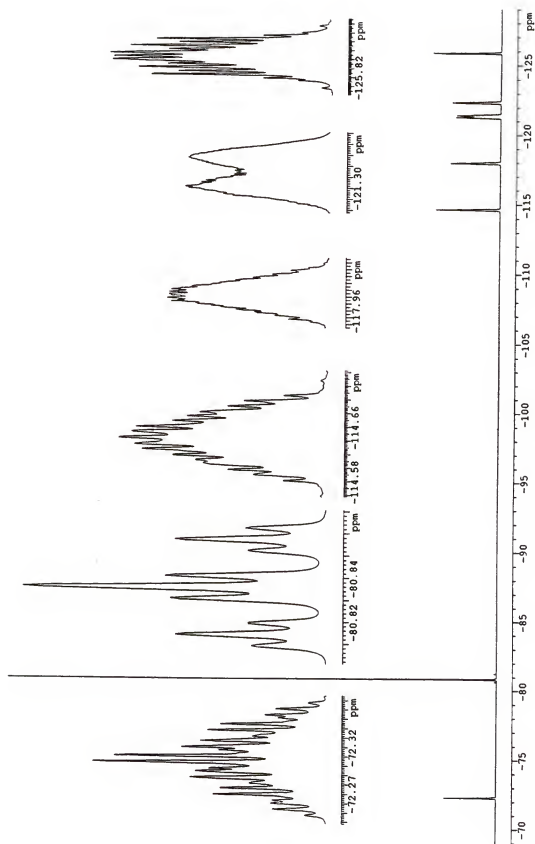
is indeed striking. We see a complicated multiplet located far downfield at -72.3 ppm, designated as *a*, with a relative area that corresponds to one fluorine nucleus. We designate the triplet of triplets at -80.8 ppm as *b*. The larger splitting in *b* is 10.2 Hz and the smaller splitting is 2.5 Hz. The multiplet at -117.9 ppm is designated *d*, and the unresolved multiplet at -125.8 ppm is labeled *g*. On the basis of their chemical shifts and relative areas, we assign *a* to the single fluorine nucleus in the dichloro-fluoromethyl group at position 1, and we assign *b* to the trifluoromethyl group at position 8. The CF₂ unit bonded directly to the terminal trifluoromethyl group in a perfluorinated chain characteristically resonates at lower frequencies than the other difluoromethylene units in the chain. So we assign *g* to the two fluorine nuclei at position 7, and using the chlorine substituent effect previously discussed in Chapter 1, we assign peak *d* to the pair of chemical shift equivalent nuclei at position 3.



IV

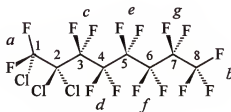
Four peaks are left to assign to positions 2, 4, 5, and 6: *c*, resonating at -114.6 ppm, two overlapping peaks, *e* and *e'*, centered at -121.3 ppm, and *f* at -122.2 ppm. Two opposing forces may affect position 2 in the chain. These fluorines are alpha to a terminal group in the chain and we have seen that this tends to place them at a relatively low frequency in the NMR spectrum. On the other hand, the fluorines at position 2 are alpha to two chlorine atoms that could shift these fluorine nuclei to a relatively high frequency in the spectrum.

Figure 2-4. One-Dimensional Spectrum of Compound IV
1,1-Dichloroperfluorooctane



Since $^3J_{cd}$ was used to determine the relative signs of $^3J_{ac}$ and $^4J_{ad}$, we can infer that the signs of $^3J_{ac}$ and $^4J_{ad}$ are opposite.

1, 2, 2-Trichloroperfluoro-octane (V). Figure 2-7 is the one-dimensional spectrum for 1, 2, 2-trichloroperfluoro-octane. It is possible to assign the unresolved multiplets at -59.2 ppm, *a*, -81.1 ppm, *b*, and -126 ppm, *g*, immediately based on their chemical shifts and relative areas. We expect a single chlorine atom, substituted for a fluorine nucleus, on a difluorochloromethyl group to deshield its fluorine neighbors. In this molecule, the additional chlorine atoms on carbon number 2 further deshield *a* to -59.2 ppm. Hence we assign *a* to the difluorochloromethyl group. The multiplet *b* is located at -81.1 ppm, where we expect to find the trifluoromethyl group at position 8. Peak *g* is located upfield at -126 ppm, where we expect to find the difluoromethylene group at position 7.



V

Peaks *c* and *d* can also be assigned on the basis of their chemical shifts and areas. Using the chlorine substituent effects, we assign the multiplet *c*, located at -107.2 ppm, to the fluorine nuclei at position 3. The broad unresolved multiplet at -116.3 ppm, *d*, is assigned to the fluorines at position 4. Both *c* and *d* have relative areas that correspond to two nuclei.

Peaks *e*, at -121.5 ppm, and *f*, at -122.4 ppm are left. The four-bond coupling in perfluorinated alkane chains can help us assign these peaks to the remaining positions in the chain: 5 and 6. Figure 2-8 shows the DQF-COSY spectrum of this molecule and

Figure 2-5. COSY/45 Spectrum of Compound IV

1,1-Dichloroperfluorooctane

SAMPLE DEC. A VI
 date Oct 19 93 dn f19
 solvent /OHL/8033- de
 /6433-cy45 dm c
 ACQUISITION dm 250
 in 4 4768 f19 temp 25.0
 at 8.129 ch PROCESSING
 up 31870.6 sb 885
 fb 17500 utfla not used
 st 32 f19
 2 f19 8132
 tpor 57 math
 pr 3.8 warr
 dl 2.000 weep
 phase 4842.0 wht
 n1 18 2020 PROCESSING
 ct lock 16 dbi 0.042
 gain 2 utflal not used
 flags n procl
 n f19 8132
 in n f19 8132
 dp hszd ACQUISITION nm up -62070.3
 sw1 31870.6 xc 31870.6
 n1 20 2839 uc 31870.6
 up1 20 2839 uc 31870.6
 up1 20 2839 uc 31870.6
 uc2 31870.6 rfi 24857.8
 uc2 31870.6 rfi 24857.8
 rfi1 24857.8 fns 1.000
 rfi1 -38012.7 al av

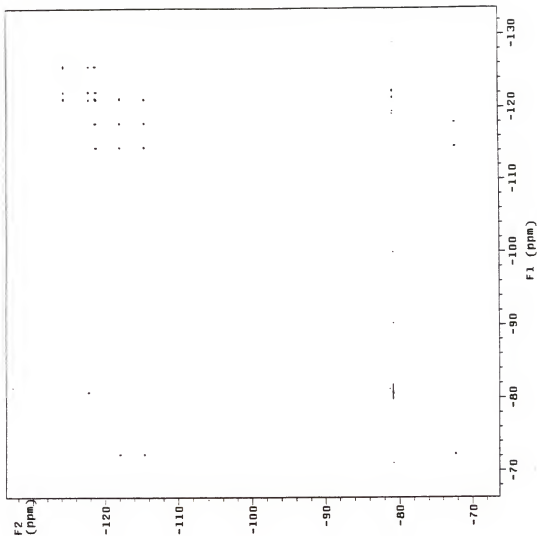


Figure 2-6. Expanded COSY45 Spectrum of Compound IV
1,1-Dichloroperfluorooctane

Figure 2-9 is an expanded view of this spectrum. Peak *a* is a convenient place to begin. We see that *a* couples to *c*, *c* couples to *e*, and *e* couples with *g* in the usual manner. We therefore assign *e* to position 5. When we trace the coupling patterns from the opposite end of the molecule, we find that *b* couples to *f* and that *f* and *d* are also coupled. This confirms that *f* should be assigned to position 6 in the chain. Moreover, we note that *f* and *c* do not couple, nor does *e* couple with *b* or *d*. So there is no evidence for the alternative assignments.

The coupling of *a* to *d*, as seen in Figure 2-8, is interesting because it extends over five bonds, and it is the most likely reason we see a second splitting of smaller magnitude in peak *a*. Peak *a* appears to be a triplet of triplets where the four-bond coupling is 8.5 Hz and the smaller five bond coupling is 2.7 Hz. We shall meet more five-bond couplings in other molecules. The geminal fluorine nuclei *d* are coupled to nuclei *c* through three bonds. The dichloromethylene group at position 2 is not as electronegative as a difluoromethylene group. So in this case, the three-bond coupling is not unexpected. On the other hand, the weak three-bond couplings between *e* and *f* and between *f* and *g* are unusual. However we have observed this particular three bond coupling between corresponding nuclei in compound IV.

Peak *b* appears to be a quartet of doublets or a quartet of triplets where the average larger splitting is 7.8 Hz. Several smaller levels of coupling in this peak are not resolved. Indeed peak *b* may have some non-first order character. It is not apparent whether the smaller splitting in peak *b* is caused by nuclei *e* or *g* in Figures 2-7 or 2-8. Peak *g* could possibly be a triplet of triplets where the larger coupling is about 14.3 Hz.

2,2-Dichloroperfluorodecane (VI). The spectrum of 2,2-dichloroperfluorodecane, shown in Figure 2-10, is similar to the spectrum of the octanes above. Many of the difluoromethylene groups in this spectrum are unresolved multiplets because each fluorine nucleus in the chain experiences many couplings of different magnitudes. Based on the expected chemical shifts, we assign the triplet of triplets *a* at -73.9 ppm to the

Figure 2-7. One-Dimensional Spectrum of Compound V

1,2,2-Trichloroperfluorooctane

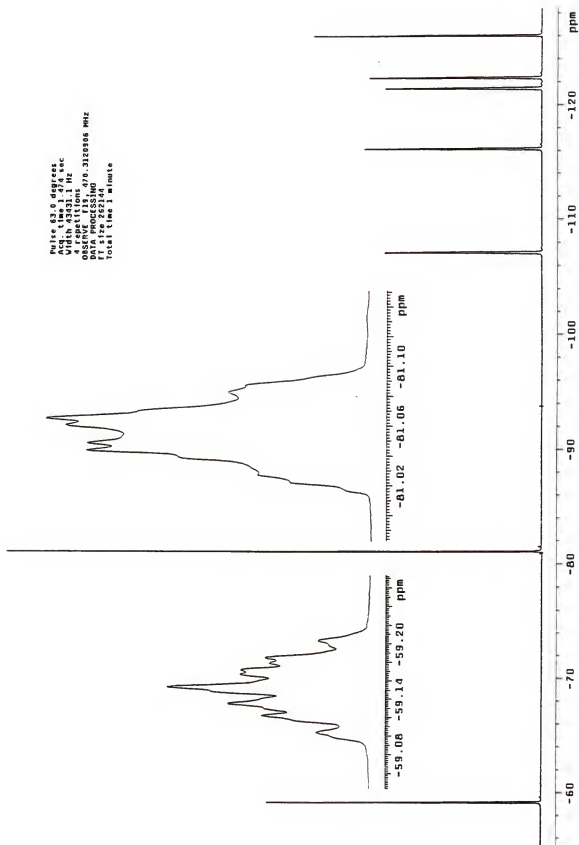


Figure 2-8. DQF/COSY Spectrum of Compound V
1,2,2-Trichloroperfluorooctane

SAMPLE DEC. & VT ACQUISITION ARRAYS
 date Oct 12 83 f19 array phase
 file /home/cyb- de nno 2000
 nml/west/dqcc038 dam c 1 phase
 ACQUISITION 260 200 1
 tfr/q 0.719 f19 temp 20.0 2
 at 0.210 9f PROCESSING 0.97
 sp 30080.4 9f not used
 fb 21500 wfile
 st 36 proc 8162
 tpr 57 math
 pr 1.55 weir react
 prstat 8418.5 wbt
 lor 0 ZD PROCESSING
 cl 0 wfile
 alock n 9f 0.013
 gain flags n initial not used
 tt n precl ft
 dn n fml display 4086
 ht yn sp -63071.5
 tssut ACQUISITION y wp -30806.4
 twi 30806.4 xc 36
 nl Phase arrayed 145
 Phase arrayed 145
 spl ZD Displayed 200.0
 spl -63071.5 rfi 24951.6
 wpi 30806.4 rfp -30811.8
 wci 145 lnc 1.000
 rfi 24951.6 at ph
 rfp -30811.8

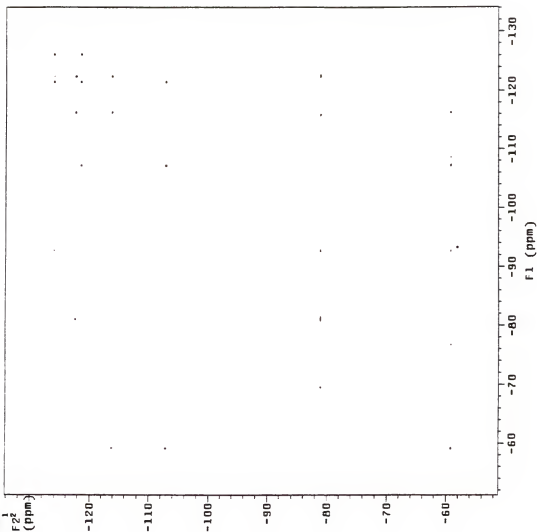


Figure 2-9. Expanded DQF-COSY Spectrum of Compound V
1,2,2-Trichloroperfluorooctane

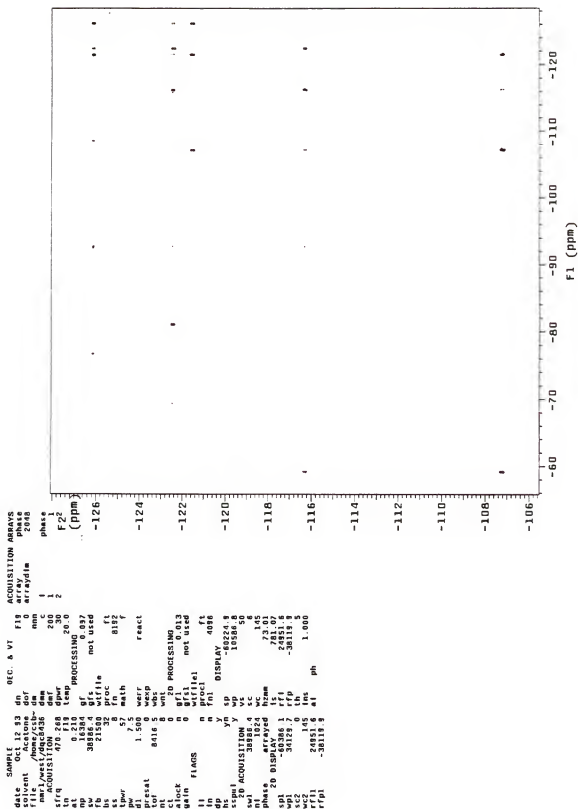


Figure 2-9 is an expanded view of this spectrum. Peak *a* is a convenient place to begin. We see that *a* couples to *c*, *c* couples to *e*, and *e* couples with *g* in the usual manner. We therefore assign *e* to position 5. When we trace the coupling patterns from the opposite end of the molecule, we find that *b* couples to *f* and that *f* and *d* are also coupled. This confirms that *f* should be assigned to position 6 in the chain. Moreover, we note that *f* and *c* do not couple, nor does *e* couple with *b* or *d*. So there is no evidence for the alternative assignments.

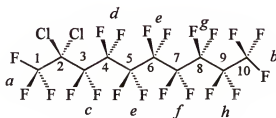
The coupling of *a* to *d*, as seen in Figure 2-8, is interesting because it extends over five bonds, and it is the most likely reason we see a second splitting of smaller magnitude in peak *a*. Peak *a* appears to be a triplet of triplets where the four-bond coupling is 8.5 Hz and the smaller five bond coupling is 2.7 Hz. We shall meet more five-bond couplings in other molecules. The geminal fluorine nuclei *d* are coupled to nuclei *c* through three bonds. The dichloromethylene group at position 2 is not as electronegative as a difluoromethylene group. So in this case, the three-bond coupling is not unexpected. On the other hand, the weak three-bond couplings between *e* and *f* and between *f* and *g* are unusual. However we have observed this particular three bond coupling between corresponding nuclei in compound IV.

Peak *b* appears to be a quartet of doublets or a quartet of triplets where the average larger splitting is 7.8 Hz. Several smaller levels of coupling in this peak are not resolved. Indeed peak *b* may have some non-first order character. It is not apparent whether the smaller splitting in peak *b* is caused by nuclei *e* or *g* in Figures 2-7 or 2-8. Peak *g* could possibly be a triplet of triplets where the larger coupling is about 14.3 Hz.

2,2-Dichloroperfluorodecane (VI). The spectrum of 2,2-dichloroperfluorodecane, shown in Figure 2-10, is similar to the spectrum of the octanes above. Many of the difluoromethylene groups in this spectrum are unresolved multiplets because each fluorine nucleus in the chain experiences many couplings of different magnitudes. Based on the expected chemical shifts, we assign the triplet of triplets *a* at -73.9 ppm to the

terminal CF_3 at position 1, and assign the other triplet of triplets, *b*, at -81.1 ppm, to the trifluoromethyl group at position 10, the opposite end of the molecule. The larger splitting in peak *a* is 12.5 Hz, and the smaller splitting is 6.3 Hz. The larger splitting in *b* is 10.3 Hz and the smaller splitting is about 2.1 Hz.

The resonance at -126.1 ppm, designated *h*, is assigned to the two fluorine nuclei in position 9. Using the chlorine substituent effect, we expect the resonance *c*, at -109.3 ppm to be the difluoromethylene group at position 3, and we expect *d*, at -116.4 ppm, to be the CF_2 group at position 4.



VI

As with the previous molecules, we can use the four-bond coupling pattern characteristic of perfluorinated molecules to assign the remaining peaks at -121.2 ppm, *e*, at -121.6 ppm, *f*, and *g* at -122.5 ppm. In Figure 2-11, the correlation spectrum, we observe a crosspeak between peaks *h* and *f*, and one between peaks *b* and *g*. Since *f* does not couple to *b*, we assign *f* to the fluorines at position 7 and we assign *g* to the fluorines at position 8. The remaining resonance, *e*, has twice the area of peaks *c*, *d*, *f*, *g*, or *h* respectively, and we are left to assign the fluorines at positions 4 and 5 in the chain. We might expect that the *e* fluorines are vicinal to each other. Assigning *e* to the two middle difluoromethylene groups at positions 5 and 6, explains the crosspeaks between *e* and *d*, between *e* and *c*, between *e* and *f* and between *e* and *g*. The fluorines at position 6 couple with the *d* and *g* fluorines, and those at position 5 couple with the *c* and *f* fluorines. Both

Figure 2-10. One-Dimensional Spectrum of Compound VI
2,2-Dichloroperfluorodecane

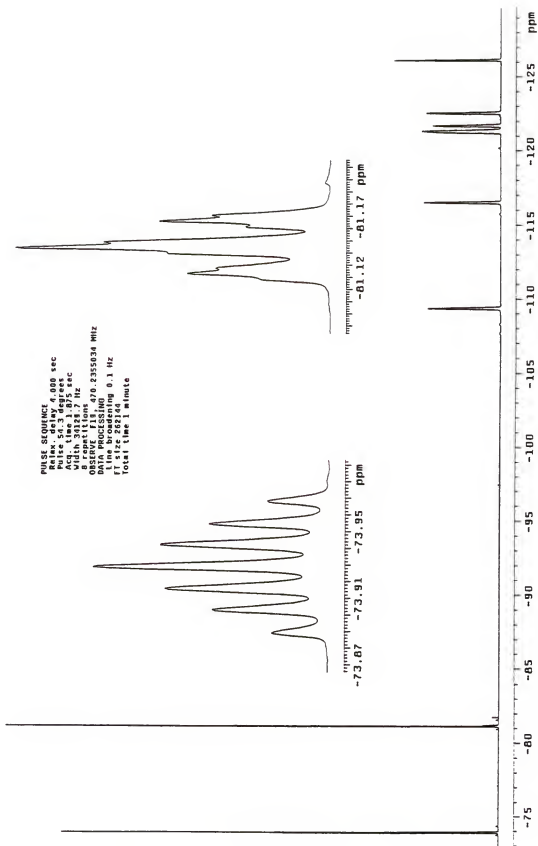
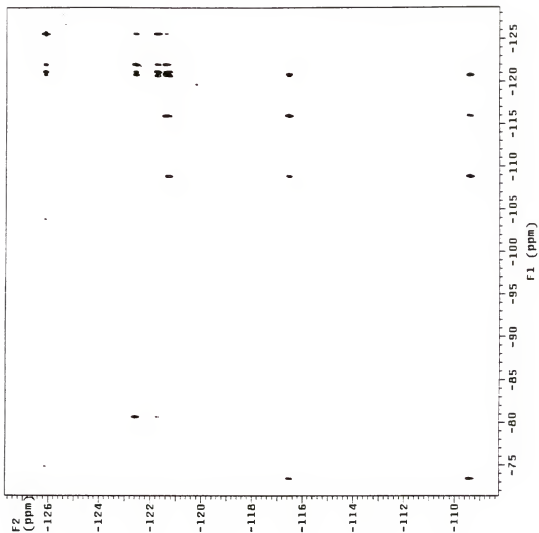


Figure 2-11. COSY45 Spectrum of Compound VI
2,2-Dichloroperfluorodecane

Figure 2-12. Expanded COSY45 Spectrum of Compound VI
2,2-Dichloroperfluorodecane

data SAMPLE DEC. & VI
 solvent DC 3 AS 483.754
 file /opt/834- dpor 48
 ACQUISITION 545 dof num 0
 sffrq 470 198 dm w
 in 6 f19 dar 10000
 np 6192 drat 1.0
 sw 34128.7 homo 25.0 n
 bt 18600 temp PROCESSING 25.0
 ss 84
 ts 8 tb 0.080
 tpor 61 sbc
 pl 3.1 proc f1
 dl 4.000 fn 8182
 nt 60848 math f
 cl 8 wevr react
 tnu 0 wep
 relay 0 wnt
 gain 0 2D PROCESSING
 in 0 sbt 0.015
 fl 0 wtfail not used
 bt 0 proc1 f1
 8182
 2D ACQUISITION
 swl 34128.7
 phase 162.6
 sp DISPLAY
 wp -8136.6
 vs 1000
 cc 145
 hzom 179.51
 lc 201.09
 rfp -33847.7
 th 0
 at cdc av 1.000
 2D DISPLAY
 sp1 -8092.3
 sc2 2092.0
 wcr 201.145
 rfp1 -33847.7

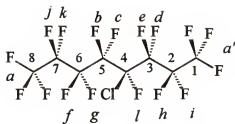


c and *d* correlate with *a*, confirming the assignments. As in compounds IV and V, there exists some coupling between vicinal fluorines. The two chlorine atoms at position 2 facilitate the vicinal coupling between nuclei *c* and *d*. There is also a crosspeak between peaks *g* and *h*, another set of fluorine atoms that are three bonds apart. Molecular simulations show that the end of the chain farthest away from the chlorine substituents in each of the molecules IV, V, and VI, has a wagging vibration with a large amplitude. Perhaps this wagging motion contributes to this trend of three-bond coupling.

A five-bond coupling between *a* and *d* is also evident in Figures 2-10 and 2-11. We have seen a five-bond coupling for the corresponding positions of compound V, but the five-bond coupling here is unusually large. Another five-bond coupling is found between peaks *e* and *h*. We find still another five-bond coupling between nuclei *b* and *f*. As in compound IV, it is located away from the chlorine atoms at the opposite end of the molecule.

We can say a little more about the five-bond coupling between *b* and *f* in this molecule. A vector drawn through the center of the crosspeak between *e* and *f* in Figure 2-12 subtends an angle, ϕ_{ef} , with the diagonal that is smaller than 45° . This implies that the coupling constants $^5J_{bf}$ and $^4J_{fh}$ have the same sign. A similar angle ϕ_{cd} , for the crosspeak between *c* and *d*, is also smaller than 45° , indicating that the coupling constants $^4J_{ac}$ and $^4J_{ce}$ also have the same sign.

4-Chloroperfluoro-octane (VII). The one-dimensional spectrum for this molecule is shown in Figure 2-13. The single chlorine atom near the middle of the perfluorinated octane chain causes each difluoromethylene group in the spectrum to exhibit a separate AB pattern. It is normal to see inequivalent geminal fluorine nuclei for the difluoromethylene groups alpha and beta to a chiral center, but position 7 in this molecule is more distant and it is unusual to see an AB pattern for fluorine nuclei so far distant from the center.



VII

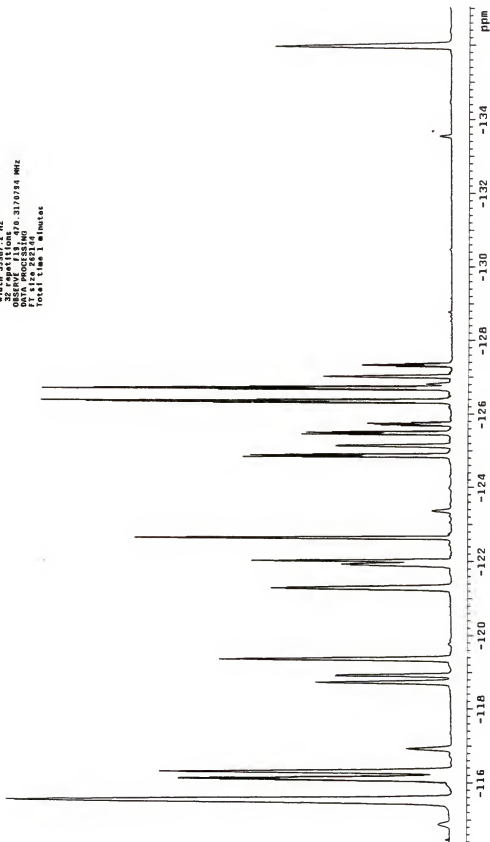
At -80.6 ppm, the two overlapping multiplets designated as *a* and *a'* are assigned to the trifluoromethyl groups. This multiplet is expanded above the spectrum in Figure 2-13. We see that this is a superposition of two peaks: *a* is a triplet of triplets, and *a'* is a triplet of doublets. The larger splitting in *a* is 10.3 Hz and the smaller splitting is 2.5 Hz. For *a'*, the larger splitting is 11.9 Hz and the small splitting is 1.9 Hz. These first order patterns are an example in which five-bond rather than vicinal coupling is observed in perfluorinated carbon molecules. That the smaller splitting (1.9 Hz) in one triplet is only a doubling indicates that it arises from a five-bond coupling between the fluorine at position 4 and the trifluoromethyl group at position 1. On the opposite half of the molecule we observe a 2.5 Hz coupling to a difluoromethylene group, evidently at position 5, five bonds away from the corresponding trifluoromethyl substituent, rather than at position 7. This is noteworthy because it is not often that we are able to resolve several levels of coupling to the terminal fluorine nuclei. The triplet at -80.9 ppm is an impurity.

The difluoromethylene and chlorofluoromethylene region is expanded in Figure 2-14. There are two overlapping AB patterns between -113.6 and -116.2 ppm. The inner legs for one of these AB patterns almost coincide at -114.5 ppm. We designate nucleus *b* as the downfield doublet in the first AB pattern centered at -114.5 ppm. At approximately -113.9 ppm, 294.2 Hz away, we observe the outer leg for this doublet. Its intensity is only 6.7% of the inner peaks and we would expect that the corresponding outer leg for upfield doublet in this AB pattern--the doublet that we designated *c*--would have an intensity

Figure 2-13. One-Dimensional Spectrum of Compound VII
4-Chloroperfluorooctane

Figure 2-14. Expanded One-Dimensional Spectrum of Compound VII
4-Chloroperfluorooctane

PULSE SEQUENCE
Pulse program 1, 580 sec
Pulse 63.0 degrees
Acq. time 1.318 sec
SOLVENT CDCl₃ 77
32 repetitions
OBSERVE F13, 478.3170754 MHz
DATA PROCESSING
FT 5149.283146
Total time 1 minutes



similar to the peak at -113.9 ppm. We do not see this small peak because it overlaps with the more intense AB pattern for nuclei *d* and *e*. The doublet labeled *d* is located at -115.1 ppm. Just as part of the doublet for *c* lies underneath larger peaks, the corresponding outer leg for *d* is hidden underneath the more intense inner resonance for the AB pattern designated *b* and *c*. The upfield half of this AB pattern is located at -116.0 ppm and is designated as *e*. Its outer leg has 17% of the intensity of the inner peak and is located 293.2 Hz upfield.

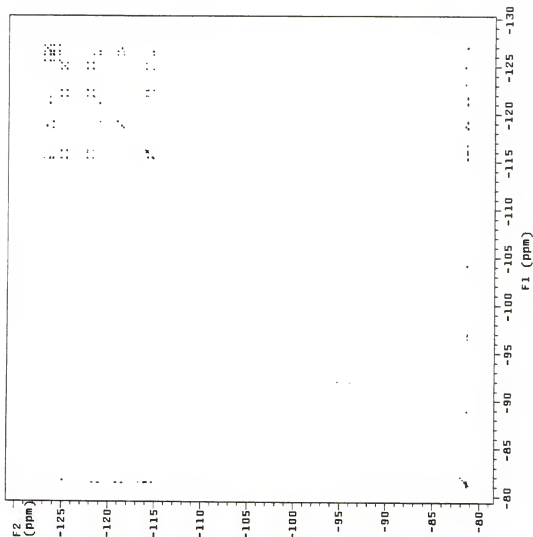
Two more overlapping AB patterns are between -117.0 and -124.1 ppm: one is located at -118.1 and -120.6 ppm, *fg*, and the other is found at -121.4 and -124.1 ppm, *hi*. Nuclei *f* and *g* are strongly coupled by 298.3 Hz in the former AB pattern, while *h* and *i* are coupled to each other by 295.3 Hz in the latter AB pattern. We find, unobscured, still another AB pattern in the spectrum with nuclei *j* and *k*, at -125.2 and -125.9 ppm coupled by 297.2 Hz. The peaks at -117.9 ppm and -124.1 ppm are an impurity

The two AB patterns located at highest frequencies, *bc* and *de*, are assigned to the fluorines at positions 3 and 5, close to the chlorofluoromethylene group. Since they adjoin trifluoromethyl groups, positions 2 and 7 should correspond to the two AB patterns at lowest frequencies, *hi* and *jk*. Position 2 should be more unshielded by the chlorine atom than position 7, so we assign *hi* to position 2, at higher frequency, and *jk* to position 7 at lower frequency. In the correlation spectrum, Figure 2-15, nuclei *d* and *e* are coupled to *i* and *h*, therefore we assign *d* and *e* to the inequivalent fluorine nuclei in the difluoromethylene unit at position 3. The remaining AB pattern *f, g* is assigned to position 6.

The average chemical shift difference in the AB patterns beta to the chiral carbon, *fg* and *hi*, is 1234.8 Hz. This difference is 858% larger than the average chemical shift difference for the AB patterns found in *bc* and *de*, located on the carbon alpha to the chiral center. Furthermore, this difference is 258% larger than that of *jk*, the AB pattern on the carbon gamma to the chiral center. So it appears that the geminal fluorine atoms on the

Figure 2-15. COSY Spectrum of Compound VII
4-Chloroperfluorooctane

SAMPLE 25.53 dn fig
 date Oct C0C13 dor
 solvent /opt/8888-dm nan
 file /opt/8888-dm 25.53
 ACQUISITION 470.268 dpr 30
 sfrq 0.718 leap 25.0
 nt 16 20 PROCESSING 0.115
 np 16394 sb not used
 sw 35507.2 sb not used
 bw 19802 wf file fl
 ss 2 fn 16384
 tpr 57 math f
 pl 3.8 warr react
 dl 2.000 wexp
 tot 3247.8 wnt
 nt 16 20 PROCESSING 0.042
 nt 16 20 PROCESSING 0.042
 gain flads n sbfl not used
 fl 0 wf file fl
 in n fl DISPLAY 8132
 dp n y sp -6134.8
 nt 20 ACQUISITION 285.590
 sw1 35507.2 ac 16
 nt 20 ACQUISITION 285.590
 sw1 35507.2 ac 16
 sp1 -61268.9 is 168.09
 sp2 -61268.9 is 201.07
 w2 23333.0 rfp -35088.3
 w2 320145 th
 rfp1 -35088.3 ins 1.000
 av



carbon beta to the chiral center form the AB pattern with the largest chemical shift inequivalence.

It is curious to see that some crosspeaks in the correlation spectrum are more intense for one geminal partner in the AB pattern. For example, in Figure 2-16 the geminal fluorines, *d* and *e*, are correlated to *b* and *c* with equal strength, but the crosspeak between *e* and *i* is much more intense than the crosspeak between *d* and *i*. We do not observe a crosspeak between *e* and *h*, nor do we see one between *e* and *j* at the vertical scale level used in Figures 2-15 and 2-16. However, we do observe a weak crosspeak between *d* and *j*. Furthermore there is a crosspeak of moderate intensity between *f* and *j*, but the intensity of the crosspeak between *f* and *k* is rather weak.

If this molecule was floppy, we might expect that all the crosspeaks among the geminal partners have the same intensity. That this is not the case is an indication that this molecule is rather rigid, perhaps in an extended confirmation. A molecular dynamics simulation also supports this conclusion.

Furthermore, as we discussed in the first chapter, the nuclear spin-spin coupling may, in part, be transmitted through the interaction of non-bonding orbitals⁵⁶ when the two coupled nuclei are close in space. This through space mechanism for spin-spin coupling may also be part of the reason for the preference in the manifestation of J coupling observed here. Although there is some uncertainty in this argument, we used the different intensities associated with the crosspeaks for the geminal fluorine nuclei *d* and *e*, *j* and *k*, and *h* and *i*, as the basis for the specific assignments to the individual inequivalent geminal fluorine nuclei in this molecule.

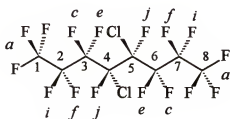
The impurity peaks in the spectra of this molecule belong to a single molecule. Figures 2-15 and 2-16 show that these three peaks: a triplet of triplets at -81.8 ppm, an unresolved quartet at -118.9 ppm, and an unresolved multiplet at -125.1 ppm, are correlated.

Figure 2-16. Expanded COSY Spectrum of Compound VII
4-Chloroperfluorooctane

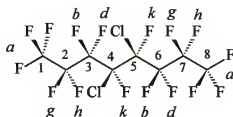
Mixtures of Chlorofluoro-Alkanes

Many of the methods used to synthesize fluorocarbons result in isomeric mixtures that are very difficult to separate. NMR holds some promise for identifying the compounds in the mixtures. In this section, we extend the information that we learned in analyzing a single compound to characterizing the compounds in a mixture.

Mixture of 4,5-dichlorohexafluoro-octanes. It is apparent that Figure 2-17 and Figure 2-18 are the one- and two-dimensional spectra of a mixture of configurational isomers. There are two overlapping AB patterns between -110.0 and -115.0 ppm, two more overlapping AB patterns between -121.0 and -124.5 ppm, and two complicated, unresolved multiplets that take on the appearance of broad singlets further upfield at -127.6 and -128.3 ppm. The spectrum from a single diastereomer below should result in a total of two AB patterns and a single peak upfield containing unresolved fine structure because of molecular symmetry. The two principal isomers were reported to be in the mixture at equal concentrations so the numerous peaks of weak intensities must belong to impurities. Then the challenge is to associate the individual resonances with a specific molecule.



VIII



IX

The four fluoromethyl groups, designated *a* for the two in each isomer, resonate at -81.2 ppm. Peak *a* is tripled because it is coupled to the fluorines at positions 3 and 6 in molecule VII and IX. Figure 2-18, the correlation spectrum, shows cross-peaks for *a* with each of the two AB patterns downfield. The doublets in the first AB pattern are

Figure 2-17. One-Dimensional Spectrum of 4,5-Dichlorohexafluorooctanes
Compounds VIII and IX

UNITYplus-500 "cebmwrl"
PULSE SEQUENCE
Relax delay 1.500 sec
Pulse 63.0 degrees
Sweep 1200 Hz
Width 39211.5 Hz
64 repetitions
OBSERVED F1 470.3180545 MHz
DATA PROCESSING
FT size 262144
Total time 4 minutes

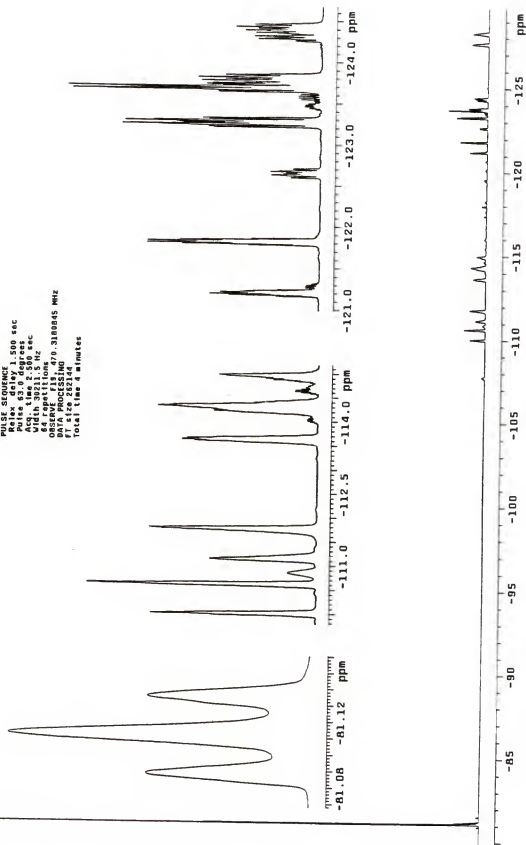


Figure 2-18. DQF COSY Spectrum of 4,5-Dichlorohexafluorooctanes
Compounds VIII and IX

designated *b* and *d*. Their chemical shifts are -110.3 and -113.9 ppm, and they are coupled by 290.2 Hz. The second AB pattern, at -111.5 and -114.6 ppm and labeled *c* and *e*, belongs to the other molecule. These nuclei are coupled by 293.4 Hz. The small peak at -110.8 ppm is an impurity.

The chemical shift values for these AB patterns and coupling to *a*, seen from the correlation spectrum, suggest that they arise from the difluoromethylene units at positions 3 and 6, alpha to the chlorofluoromethylene groups in *each* of the two molecules. The two such difluoromethylene groups in each isomer are chemical shift equivalent, so that nuclei corresponding to peaks *b* and *d* belong to two CF₂'s of one molecule, and those corresponding to *c* and *e* belong to the two CF₂'s in the other molecule.

Two more overlapping AB patterns occur near -121.0 and -124.5 ppm. Resonances *f* and *i* comprise one AB pattern coupled by 285.2 Hz and have the chemical shifts of -121.4 ppm and -124.1 ppm. Resonances *g* and *h* are coupled by 293.9 Hz in an AB pattern with a relatively small chemical shift dispersion. So we find the smaller AB pattern, *gh*, inside the AB pattern containing nuclei *f* and *i*. Resonance *g* is located at -123.1 ppm and is unobscured by any overlapping peaks. The chemical shift for the doublet *h* is -123.9 ppm. This doublet overlaps the small doublet *z*, but it is distinguishable in both the one- and two-dimensional spectra. The appearance of these AB patterns could cause one to associate *f* with *h*, instead of with *i*, and thus misassign the resonances. So in this situation, the two-dimensional spectrum is especially helpful.

We notice in the correlation spectrum that the AB patterns containing resonances *f* and *i*, and *g* and *h* are not coupled to *a*, the trifluoromethyl groups. This observation together with their chemical shifts suggests that these AB patterns arise from the difluoromethylene groups at positions 2 and 7 alpha to these trifluoromethyl groups, one pattern arising from each isomer.

The resonances arising from chlorofluoromethylene groups fall to slightly higher fields than those of difluoromethylene groups. On this basis, as well as their relative areas,

we assign the resonances at -127.6 and -128.3 ppm, designated *j* and *k*, to chlorofluoromethylene groups for the two isomers. There are two such chlorofluoromethylene groups in each isomer, but the symmetry of each molecule makes the two fluorine nuclei in that molecule chemical-shift equivalent.

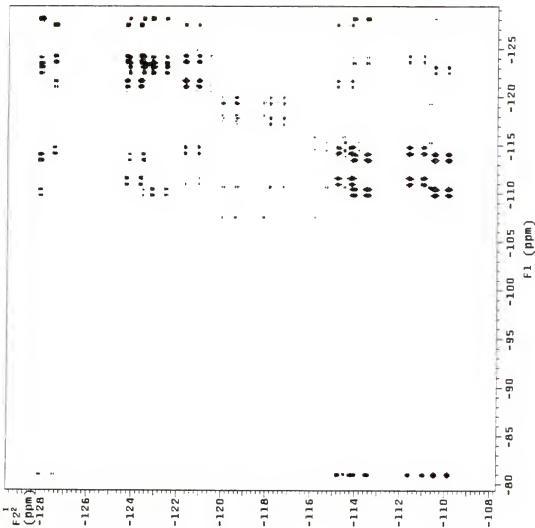
Nuclei *g*, *h*, and *d*, are coupled to *k*, and nuclei *i* and *f* are coupled to *j*. By tracing out their separate correlation spectra in Figures 2-18 and 2-19, we can distinguish the two isomers. Thus the fluorine nuclei corresponding to peaks *b*, *d*, *g*, *h* and *k* arise from one molecule, and those fluorines corresponding to peaks *j*, *i*, *f*, *e*, and *c* belong to the other isomer. Moreover certain nuclei appear to couple to one geminal partner more intensely than they do to the other. For example, we only barely detect a crosspeak between *k* and *b*, the strongly coupled geminal partner of *d*, after we increase the vertical scale of the spectrum by a factor of ten. Likewise, coupling between *g* and *d* is not apparent in Figure 2-19 with the scaling factor used, but *g* is weakly coupled to *b*. A similar uneven distribution of crosspeak intensities among geminal partners is in the spectrum of the isomer. Peak *j* is more intensely coupled to *i* than it is coupled to *f*. Peak *j* is also very weakly coupled to *e*, and, at an increased vertical scale, one can barely detect the extremely weak J-coupling between *j* and *c*. Peak *i* is weakly coupled to *c*, and the coupling to its geminal partner *e* is even weaker, but perceptible. Peak *f* appears to couple with *e* weakly, but we do not see it couple to *c*.

As in compound VII, molecular dynamics simulations indicate that these diastereomers stay close to an extended geometry at 300 K. Moreover, it seems reasonable that floppy molecules would have a more even distribution of crosspeak intensities; and not the uneven distribution seen in this correlation spectrum.

Although it is risky, we will use the unique coupling patterns to separate nuclei among geminal atoms to make specific assignments. As drawn above, the two chlorofluoromethylene units in compound VIII have an RS configuration, and the corresponding chlorofluoromethylene units in isomer IX have an SS configuration. For

Figure 2-19. Expanded DQFCOSY Spectrum of 4,5-Dichlorohexafluorooctanes
Compounds VIII and IX

date SAMPLE Jan 24 94 DIC. & VT
 solvent Acetone d₆ f19
 title /name/csb- dm 0
 nml /wst/ /acqsys/ 8880 def 200 1
 phase 1
 F2
 ACQUISITION 288 dpr 2
 t1:4 470 f19 tb PROCESSING 068
 at 0.135 tbs
 ap 303076 wtf file not used
 fb 18700 fn 8192 f
 ts 32 math
 tpwr 62 werr react
 pw 5 weep
 p1 5 wnt
 d1 7.000 wnt
 prstat 0 2D PROCESSING
 no 2389 6 sbi 0.000
 ct 8 wtf file not used
 alock n procl flt
 gain 0 fml DISPLAY 4096
 flags
 li n tp -60910.2
 li n v 107.10
 dp v ve 306
 hs yn sc 145
 sz 2D ACQUISITION y nc 745
 sz1 30303.0 ls 46011.59
 nt 512 rfi 4614.5
 phase arrayadd th -59959.5
 2D DISPLAYadd th 1.000
 spl -60050.7 int
 w2 25337.0 at ph
 w2 145
 r111 4815.5
 r101 -59959.2



compound IX, the single fluorine nucleus at position 4, as well as the corresponding nucleus at position 5, are on the same side of the molecule. Furthermore, these fluorine nuclei are each in close proximity to an equivalent fluorine nucleus, one at position 3 and one at position 6. In Figure 2-19, we see that the crosspeak between *j* and *e* is weaker than the corresponding crosspeak between *k* and *d* in the spectrum of the diastereomer. Provided that these molecules maintain an extended geometry, a through space transmission for the spin-spin coupling interaction in compound IX can explain this difference. If the four- and three-bond couplings in this compound have the same sign, the couplings between each of the two equivalent *k* fluorines and each of the two equivalent *d* fluorines may combine to provide a more intense crosspeak. For this reason, we place nuclei *k* and *d* on the same side of the molecule in isomer IX. Likewise, the weak three-bond coupling between peaks *b* and *g* suggests that their corresponding nuclei share the same side of compound IX.

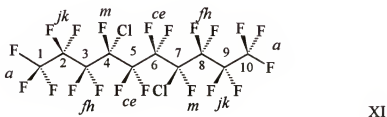
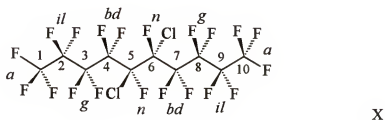
In compound VIII the crosspeaks between *j* and the geminal pair *ce* are weaker than the corresponding crosspeaks between *k* and *d* in compound IX. Because nucleus *i* is more strongly coupled to *c* in compound VIII, we place these two nuclei in close proximity. Moreover, *f* and *e* appear to couple but, even when the vertical scale is magnified 10 times, we do not find a crosspeak between *c* and *f*. Hence we have distinguished compound IX from its diastereomer VIII.

Admittedly, a through space transmission between *k* and *d*, and between the weakly correlated fluorine nuclei above, is not proven. Nonetheless, it is more reasonable to evoke a through space spin-spin coupling rather than to attribute the uneven intensities in these crosspeaks to an angular relation in through bond coupling similar to a Karplus relation.

Mixture of dichloro-perfluorodecanes

Based on their method for preparation, the chemists at the Wright-Patterson Airforce base suggested that this sample might contain one or more of the three isomers: 5,6-dichloroperfluorodecane, X, 4,7-

dichloroperfluorodecane, XI, and the asymmetrically substituted 4,6-dichloroperfluorodecane, XII. However, we see three distinct ways in which the NMR spectra in Figures 2-20, 2-21, and 2-22 can be interpreted. We will first describe the spectrum and label the peaks, then present the three interpretations as separate cases. In the first case, we present the analysis for the situation where the sample contains a racemic mixture of compound X. In the second case, we present an argument that this could be a racemic mixture of compound XI. Finally, we consider the possibility that one isomer for each of the molecules X and XI is indeed present in this mixture.



There are six AB patterns of roughly equal area in Figure 2-20, the one-dimensional spectrum of this mixture. Six AB patterns can indicate that Figures 2-20 and 2-21 are the spectra of one molecule with 12 inequivalent nuclei. Alternatively, they may indicate equal quantities of two symmetrical molecules that have pairs of chemical-shift

Figure 2-20. One-Dimensional Spectrum of Mixture of Dichloroperfluorodecanes

PULSE SEQUENCE
 Pulse delay 10.000 sec
 Pulse 90.0 degree
 Acq. time 2.000 sec
 18 repetitions
 OBSERVED F1, 476.341485 MHz
 NUC1 MASS 12.000000
 SA time 0.111 sec
 Shifted by -1.998 sec
 F1 size 28216
 Total time 3 minutes

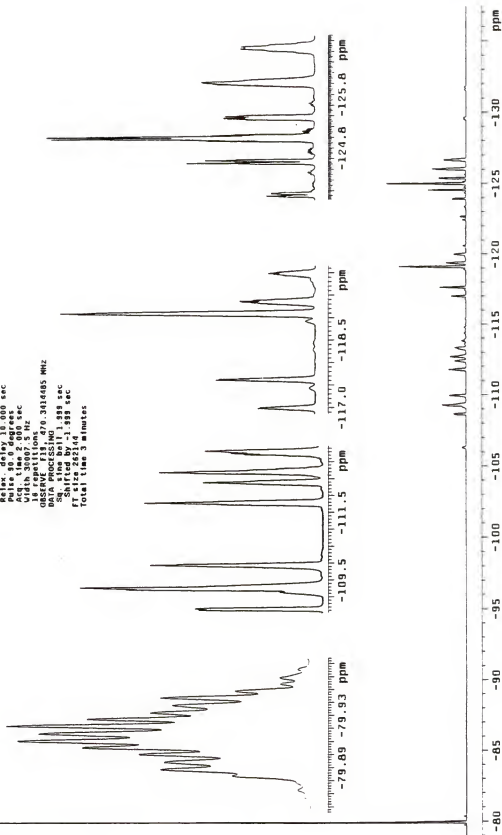


Figure 2-21. COSY Spectrum of Mixture of Dichloroperfluorodecanes

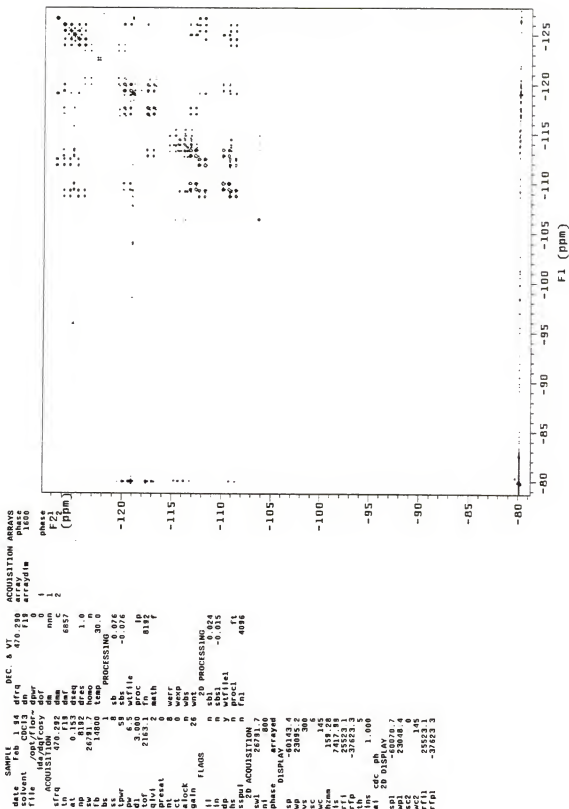


Figure 2-22. Expanded COSY Spectrum of Mixture of Dichloroperfluorodecanes

equivalent CF_2 's. Moreover, each of geminal partners for the CF_2 's in the symmetrical molecules is expected to be chemical shift inequivalent.

There are numerous small peaks in the one-dimensional spectrum. These smaller peaks indicate that another molecule is present in the mixture at much smaller quantities. For example, two smaller transitions are present at -129.5 and -131.5 ppm. This is a likely place to find a transition due to a chlorofluoromethylene group but there are no correlation peaks in the COSY spectrum associated with these small, low frequency transitions. Moreover, the number of the major peaks and their relative areas exclude isomer XII from either of the more prominent spectra in the mixture. We might expect at least four, and as many as six, distinct resonances to arise from the difluoromethylene units in isomer XII. These peaks are not observed. However, it is possible that they are present but hidden from our view due to an overlap with the AB patterns of the more abundant molecules.

In Figure 2-20, the set of peaks around -109.0 appears to be a triplet with finer unresolved coupling, but this is not the case. The two-dimensional spectrum, shown in Figure 2-21, reveals that these peaks are part of a set of overlapping AB patterns between -108.0 and -114.0. We designate the doublet at -109.0 ppm as *b*. Peak *b* is coupled to *d*, located at -112.0 ppm, in the correlation spectrum. In Figure 2-20, we see that the coupling between these two nuclei is 294.0 Hz and they have equal areas. The AB pattern overlapping with *bd* is designated *ce*. We find *c* at -109.7 ppm and its complement located at -112.9 ppm. Although the areas for *c* and *e* are slightly larger than the corresponding areas for *b* and *d*, the areas for *c* and *e* are equal. There exist a number of smaller peaks just upfield from *e*, so it is interesting to speculate that the larger areas for *c* and *e* are due to overlapping resonances from the other molecule present at smaller quantity. Indeed one of the smaller peaks upfield of *e* is correlated to the downfield side of the outer leg in the doublet *e*.

A second set of overlapping AB patterns is located farther upfield between -116.9 and -120.2 ppm. The doublet *f* is located at -117.3 ppm and its complementary doublet, *h*, is found at -119.6 ppm. They are coupled to each other by 296.7 Hz. The area for *f* is equal that of *b* and *d* individually, while the area for *h* is respectively equal to the area for each of *c* and *e*. Between *f* and *h* we find an intense resonance, *g*, with a great deal of unresolved fine structure. The area of this peak is equal to the sum of the areas for *b* and *d*. This equality suggests that the same numbers of nuclei are represented by the resonance, *g*, and the AB pattern *bd*. Upon closer examination, we see that peak *g* is actually part of an AB pattern that has nearly collapsed into an A₂ pattern. Indeed, 329.0 Hz downfield at -118.2 ppm and 329.0 Hz upfield at -119.7 ppm, we can find a set of very small doublets.

A third set of overlapping AB patterns is located between -123.0 and -126.0 ppm. A set of doublet of doublets of triplets that we designate as *i* occurs at around -124.3 ppm. The set of peaks, *i*, has an area equal to *b*, *d*, and *f*, respectively. So we conclude that each of these resonances represents the same number of nuclei. Nucleus *i* is strongly coupled to the broad doublet, *l*, located at -125.6 ppm. Part of the doublet *l*, the outer leg at lower frequency, overlaps the resonance of a single fluorine nucleus. If we subtract the area of a single fluorine from this component of *l*, we find that the adjusted area of *l* equals the area of *i*. Furthermore, we designate the peak underneath *l* as *m*. The correlation spectrum shows the AB pattern *il* is coupled to the AB pattern *bd*.

Inside the AB pattern *il* is another set of peaks, located at -124.8 and -125.1 ppm, that are arranged in an AB pattern, *jk*. The two innermost central legs of this AB pattern resemble an intense, unresolved, doublet, as in the AB pattern *g*. Moreover, one can find the very weak outer transitions associated with *jk*, 301.0 Hz away from the central transitions. Without the correlation spectrum, the AB pattern *jk* would not have been detected because the tiny outer transitions can very well be confused with peaks from the

other, less abundant, molecule in the spectrum. Crosspeaks in the COSY spectrum correlate the AB patterns *il* and *fh*.

At -126.7 ppm, we find a peak, designated as *n*, that has an area equivalent to one fluorine atom. The two-dimensional spectrum reveals correlation peaks between *n* and *g*, and between *n* and *d*.

Two distinct spectra are evident in Figure 2-21, consistent with the interpretation that there are two symmetrical molecules in this mixture as discussed under separate cases below. One of the correlation maps establishes that the resonances *bd*, *g*, *il*, and *n* arise from the same molecule. A separate set of connectivities establishes that the peaks *ce*, *fh*, *jk*, and *m* arise from a different molecule.

The trifluoromethyl groups in this spectrum resonate at the highest frequency in all the cases described below. So the pattern of overlapping triplets at -79.9 ppm, designated *a*, is assigned to the chemical shift equivalent trifluoromethyl groups in each molecule. From peak *a* we observe correlations to the AB pattern *fh* at the chemical shifts -117.3 and -119.6. There is also a correlation to the intense peak *g* at -119.1 ppm. These correlations suggest that nuclei *f*, *h*, and *g* are located four bonds away from the fluoromethyl groups.

Case 1: Racemic mixture of compound X. Considering its chemical shift and peak area, we assigned *g* to positions 3 and 8 in molecule X. Moreover, the *g* fluorines can couple well with both *a* and *n* from this position, and this coupling network is consistent with the correlation spectrum. These chemical shift arguments help to assign *il* to positions 2 and 9 in the chain and place nuclei *bd* alpha to the chlorofluoromethylene group at positions 4 and 7. Moreover, *il* and *bd* are located beta to each other--at positions 2 and 4, and 7 and 9--where the indirect nuclear coupling is effectively transmitted, consistent with what we observe in the two-dimensional spectrum.

This assignment presents two problems. Although the chlorine substituent effect places nuclei *g* at position 3 and 8, the *g* fluorines are nearly chemical-shift equivalent.

This contradicts our experience. We expect fluorine nuclei gamma to a chiral center to have a larger chemical shift difference than we see here, and the geminal fluorines beta to a chiral center should not have a very large chemical shift difference. The assignment for the AB pattern *il* is consistent with chemical shift considerations, but these geminal fluorines have a fairly large chemical shift difference. In our experience, there should be a small chemical shift difference in the geminal fluorines at this position.

The second correlation map does not fit the structure of this molecule very well either. In this alternative scheme, we would assign the slightly inequivalent geminal fluorines, *jk*, to positions 2 and 9. The fluorines forming AB pattern *fh*, would then be assigned to positions 3 and 8, and those fluorines in the AB pattern *ce* are assigned to positions 4 and 7. As we would expect, the chemical shift difference in the AB patterns *ce* and *fh* are large, but the chemical shift difference in *ce* is larger than the chemical shift difference in *fh*, and we expect the opposite to be true. Moreover, we would not expect to see a correlation peak between *ce* and *fh* in any enantiomer associated with compound X.

Case 2: Racemic mixture of compound XI. We use chemical shift arguments to assign the AB transitions, *ce*, to the two difluoromethylene units at positions 5 and 6 in the chain. At this location, the difluoromethylene unit *ce* is deshielded by *m*, the chlorofluoromethylene group that is apparent only after we examine the area of the doublet *l* very carefully. We rely, again, on our experience of the fluorine chemical shifts to assign the AB pattern *jk* to the two difluoromethylene units at positions 2 and 9, directly bonded to the terminal trifluoromethyl groups. The remaining AB pattern, *fh*, is assigned to the difluoromethylene groups at positions 3 and 8, alpha to the chlorofluoromethylene group *m* and beta to the difluoromethylene groups *ce* and *jk*. At these positions, the difluoromethylene group *fh* couples effectively with both *jk* and *ce*, providing the crosspeaks that we observe in the correlation spectrum between these peaks.

As in the previous case, there are contradicting factors in the above assignment. The fluorines in the AB pattern *jk*, have a small chemical shift difference. Since they are beta to a chiral center, we expect a large difference in the chemical shift for these geminal fluorines, and this is not the case.

The other correlation map in Figure 2-21 is an even poorer fit for this structure. Considering the chemical shifts for the multiplets in this case, we would assign the AB pattern *bd* to positions 5 and 6. Then we would assign *g* to positions 3 and 8, and the AB pattern *il* would be assigned to positions 2 and 9. However, for any enantiomer associated with compound XI, *g* should couple to *bd*. Figure 2-21 shows that *il* and *bd* are coupled, not *g* and *bd*.

Case 3: Mixture of compounds X and XI. Neither of the two cases above excludes the possibility that equal amounts of compounds X and XI are in the mixture. The assignments for these molecules do not change in this case. Moreover, the same arguments against these assignments remain.

Hence, we can not be confident about which of the three suggested isomers, or their associated enantiomers, are in the mixture.

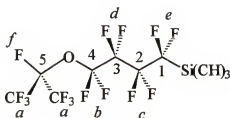
Spectra of Fluoro-Ethers

In this section, the spectra of three perfluorinated ethers are examined when they are bonded to a trimethylsilyl or an aromatic group at the beginning of the chain. The trimethylsilyl substituted chains serve as the synthetic precursors to the substituted triazine, perfluorophenyl and phenyl compounds. Rules relating the chemical shift of a fluorine nucleus to its proximity to an oxygen substituent, analogous to those that we applied to the fluorochlorocarbons, do not exist for this class of molecules. Moreover, there are far fewer AB patterns in these molecules. However, non-first order patterns are

introduced in the spectrum where a oxydifluoromethylene group is bonded to a fluoromethine unit bearing a trifluoromethyl substituent.

Trimethyl [perfluoro-4-[perfluoro-1-(trifluoromethyl)ethoxy]butyl]silane (XIII)

Figure 2-23 displays the spectrum of this molecule. There are six resonances that belong to the ether, each of which exhibits some fine structure. Several minor peaks in the spectrum are associated with an impurity. The three peaks between -119.0 and -129.0 ppm, *c*, *d*, and *e*, are located in the expected chemical shift region for difluoromethylenes. The areas of these peaks are equal, each consistent with two fluorine nuclei. A triplet, *f*, is located far upfield at -145.8 ppm, where we expect to find a fluoromethine group and its area is half that of the preceding three peaks. Despite the simple appearance of Figure 2-23, we must still use the two-dimensional correlation spectrum, shown in Figure 2-24, to assign each peak specifically.



XIII

We come across the first triplet, *a*, at -81.23 ppm. From its relative area and its chemical shift, we can assign *a* to the six equivalent fluorine nuclei in the perfluoro-isopropyl group. The relatively broad hump at -81.55 ppm, designated *b*, is where we would expect to see the difluoromethylene unit directly bonded to the ether oxygen. The relative area of *b* is representative of two fluorine nuclei, and its broad appearance indicates numerous, small, long range couplings that are not resolved. Peaks *a* and *b* are not resolved in the COSY spectrum, but as *a* is a triplet by 5.3 Hz, it is very likely coupled to *b*.

Figure 2-23. One-Dimensional Spectrum of Compound XIII

Trimethyl[1,1,2,2,3,3,4,4-octafluoro-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]butyl]silane

File: f1d
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 Relax. delay 4.000 sec
 Pulse 5d. 3 degrees
 Width 3333.3 Hz
 16 repetitions
 OBSERVED F1 F2 0.2235612 MHz
 DATA PROCESSING
 FT size 262144
 Total time 1 minutes

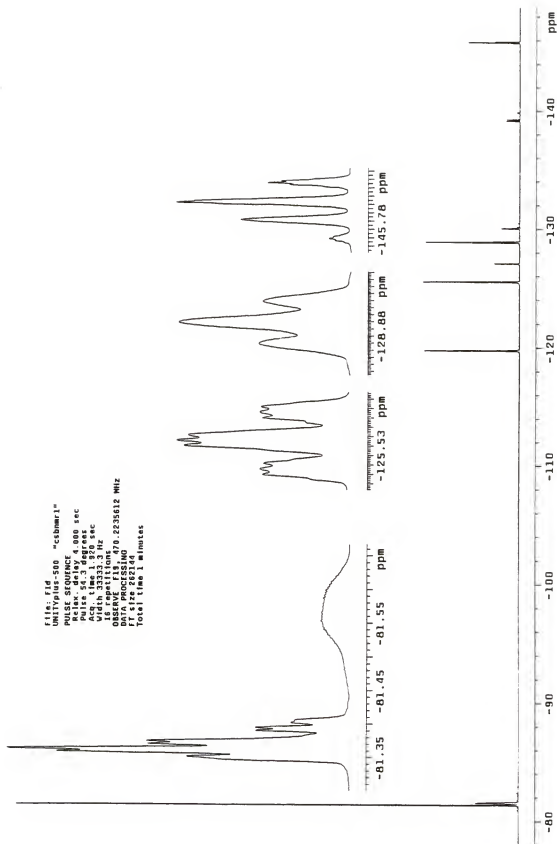
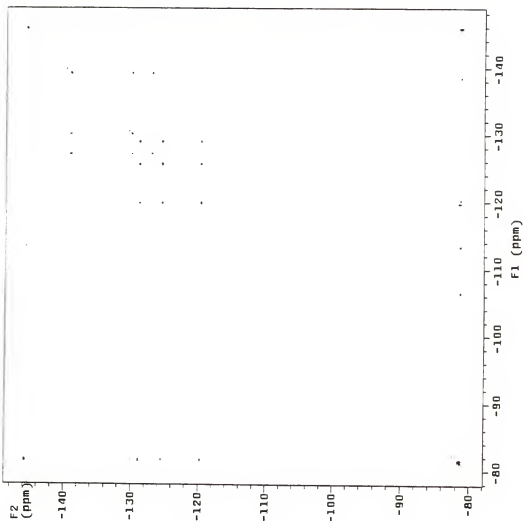


Figure 2-24. COSY Spectrum of Compound XIII

Trimethyl[1, 1,2,2,3,3,4,,4-octafluoro-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]butyl]silane

SAMPLE DEC. & VT
 date 27 85 grq 473 171
 solvent acetone dpr 140
 file /opt/1132~ dpr 40
 0
 ACQUISITION
 srfq 478 170 dmw 10000
 tn 0 f13 dmw 10000
 ct 0 f13 dmw 10000
 np 16384 dpr 1.0
 sw 33333.3 homo 1.0
 bs 18664 temp PROCESSING 25.0
 ss 8 sb 0.123
 tpr 8 sb file not used
 pl 3.1 proc ft
 d1 3.000 fm 8132
 nt -1087.8 meth f
 ct 8 werr react
 relay 0 weep
 alock 0 weep
 gain 5 sb 2D PROCESSING
 fls n sb1 8132
 li n sb1 not used
 in n wt/fil
 ds n proc
 hs yn fm 8132
 2D ACQUISITION
 srfq 473 171
 nt 33333.3
 phase 2048
 sp display 0
 sp 4971.1
 wp 33333.3
 vs 500
 vc 142
 hznm 128.74
 f1 128.74
 rf1 9366.1
 rfp -60605.0
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 sc2 142
 rf1 9366.1
 rfp1 -60605.0



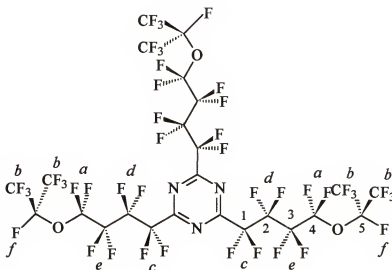
In the COSY spectrum we observe a correlation peak between *c*, the broad resonance at -119.8 ppm, and the overlapping peaks in the area of -81.5 ppm. It is probable that it is *b* that is coupled to *c* rather than *a*, because *a* is located far away from position 2 in the chain. *a*. Peaks *c* and *d* are also correlated. There exists a 14.0 Hz separation in the triplet, labeled *d* at -125.5 ppm. Peak *e*, located at -128.9 ppm, is also a triplet whose fine structure is split by 13.8 Hz. Moreover a crosspeak exists between these two triplets.

Since *e* is shielded to greater degree than the other difluoromethylene nuclei, we assign *e* to position number 1, bonded directly to the electropositive trimethylsilyl group. We assign *d* to the fluorine nuclei on carbon number 3 because *d* and *e* are tripled by the same coupling constant. Peak *c* is assigned to position 2 where it may couple with both *b* and *e*. That the vicinal fluorines *c* and *d* couple is consistent with the relationship previously discussed between vicinal fluorine coupling and the electronegativity of the other substituents bonded to the adjacent carbon atoms. Therefore this assignment is consistent with what we know about the behavior of chemical shifts and coupling constants in perfluorinated molecules.

Peak *f* is located at -145.8 ppm and tripled by 21.3 Hz. The relative area of *f* is consistent for one fluorine nucleus. From the two-dimensional spectrum we observe a crosspeak between *f* and the overlapping peaks, *a* and *b*. Since *f* is not a septet, we know that the larger indirect coupling is with *b*. The coupling constant between *f* and *b* is nearly twice as large across the ether oxygen in this molecule as that which we normally see for fluorine four-bond coupling.

2,4,6-Tris [perfluoro-4-[perfluoro-1-(trifluoromethyl)ethoxy]butyl]-1,3,5-triazine (XIV). Compound XII was used as a reactant in synthesizing compound XIV. The one-dimensional spectrum for this molecule is shown in Figure 2-25. The general appearance of this spectrum differs from the spectrum of its precursor molecule in Figure 2-23, although we observe resonances at roughly similar locations. However, the assignments

of the respective peaks do change. The most curious effect is that the broad hump and triplet, labeled *b* and *a* in the preceding spectrum, have been transposed in this spectrum. We assign the broad hump at -81.1 ppm, *a*, to the oxydifluoromethylene group at position 4 in the chain, and we assign the trifluoromethyl group to the triplet at -81.5 ppm, *b*. This molecule required an acetone-*d*₆/freon-113 mixed solvent system, while molecule XII goes into acetone without any other solvents. So it is not clear whether we are witnessing the effects of the solvents or the effects of the triazine ring. Moreover, it is not clear why either the solvent or the triazine ring should transpose these resonance frequencies.



XIV

As in Figure 2-23, the spectrum of the precursor, the fine structure in the CF₃ resonance is split by 5.3 Hz. We find some overlap between peaks *a* and *b* in Figure 2-26, the two-dimensional spectrum, but presumably the two *a* fluorine nuclei cause the tripling. We also expect that it is the CF₂ group at position 4 in the chain, *a*, that is correlated to *f*, the fluoromethine fluorine nucleus at -145.7 ppm, as it is in the precursor. Peak *f* displays a large 21.3 Hz coupling constant, which is also what we saw in the precursor. Moreover, peak *f* is also correlated with peak *b*.

Figure 2-25. One-Dimensional Spectrum of Compound XIV

2,4,6-Tris[1,1,2,2,3,3,4,4-octafluoro-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]butyl]-1,3,5-triazine

PULSE SEQUENCE
Relax delay 3.500 sec
Pulse 5d 5 degrees
AQ 4 sec 1.000 sec
Width 4443.4 Hz
32 repetitions
OBSERVE F18, 470.223335 MHz
SOLVENT CDCl₃
FT size 262140
Total time 2 minutes

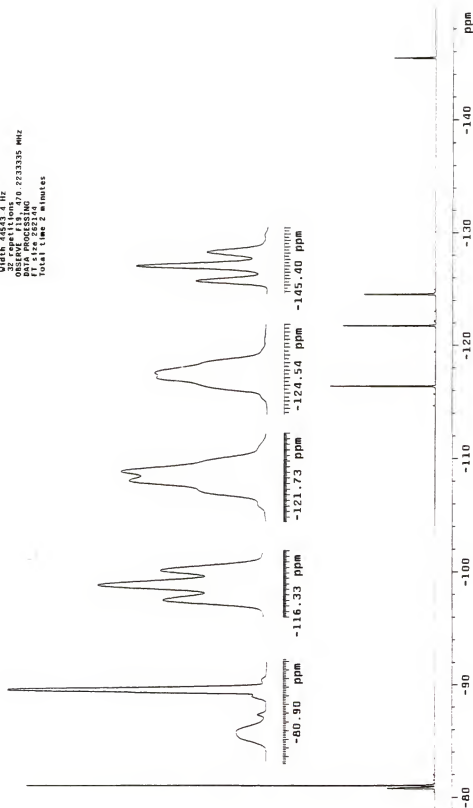
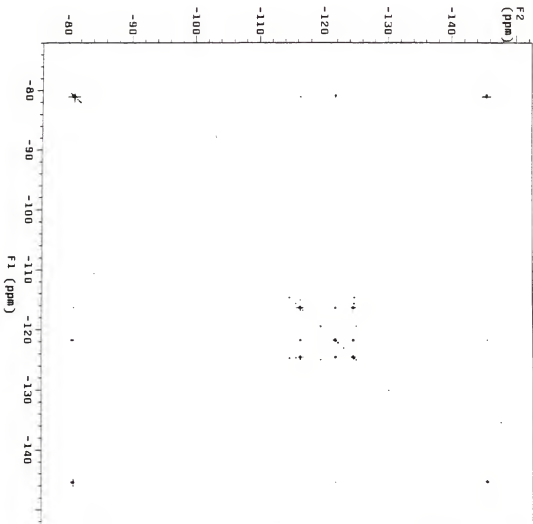


Figure 2-26. DQF-COSY Spectrum of Compound XIV
2,4,6-Tris[1,1,2,2,3,3,4,4-octafluoro-4-[1,2,2,2-tetrafluoro-1-(trifluoromethyl)ethoxy]butyl]-1,3,5-triazine

```

SAMPLE 30.95 REC. 6 VT
date 06/05/93 dtrq 470.146
solvent /home/csb-dwr 40
nmr/inst/seq/254280 -254280nm
nmr/inst/seq/cy945 da
=====
ACQUISITION
f1 470.173 dnm 10000
tq 470.173 dreq 1.0
at 0.184 dres 1.0
nu 445334 hnum 7
fb 24600 hsum 25.0
=====
PROCESSING
ls 64 sb 9.082
ss 32 sb 1.000
tpw 61 wfile
pw 6.3 proc ft
pc 3.1 f2 ft
d1 3.500 math 8192
=====
tqf -95.3 werr react
tqf 10.0 werr
ct 8 werr
lax 0 werr
creay 0 werr
atock n werr
=====
ZB PROCESSING
uain flags 4 sb1 0.923
ii flags n sb1 not used
in flags n wfile ft
=====
ZB ACQUISITION
sol 445334
nu 24600
fb 24600
=====
phase 0
=====
SP DISPLAY
sp -71635.6
vc -35881.4
vc 560
vc 560
wc 307.145
hnum 100.000
f1 40130.3
f1p -33946.4
tq 10.0
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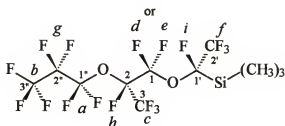


The triplet, *c*, located at -116.3 ppm, is further downfield than we normally see difluoromethylene units. Hence we assign *c* to position 1 in the chain, directly bonded to the triazine ring. A crosspeak between *c* and the multiplet *e*, located at -124.6 ppm, identifies *e* as the difluoromethylene group at position 3 in the chain.

The remaining multiplet, located at -122.4 ppm, *d*, is assigned to the two fluorine nuclei on the number 2 carbon in the chain. The COSY spectrum, in Figure 2-26, confirms this assignment by revealing a crosspeak between *d* and *a*.

Trimethyl[perfluoro-1-[perfluoro-2-(perfluoropropoxy)propoxy]ethyl]silane (XV).

In the two spectra of XIII and XIV shown in Figures 2-23 and 2-25, the oxydifluoromethylene groups appear as a relatively broad hump of low intensity. In the one dimensional spectrum of this molecule, Figure 2-27, there are three, complex, non-first order patterns that overlap more intense multiplets. The AB pattern *a* is centered at -77.3 ppm. The multiplet labeled *d* is centered at -80.0 ppm, and a third multiplet, *e*, is centered at -81.3 ppm. We will assign these multiplets to the oxydifluoromethylenes in the compound XV. As there are only two such substituents drawn below, the third multiplet must be a consequence of an enantiomer of this molecule.



XV

We shall designate the triplet at -78.0 ppm, overlapping the unresolved multiplet *a*, as *b*, and, because of its chemical shift, we assign *b* to the trifluoromethyl group terminating the molecule at position 3'' of the propoxy substituent. We would expect the chemical shift of the oxydifluoromethylenes at position 1'' to be similar to that of *b*.

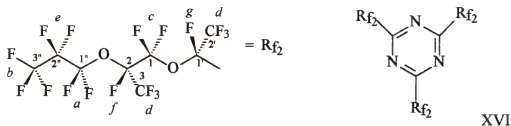
Figure 2-27. One-Dimensional Spectrum of Compound XV
Trimethyl[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-silane

Therefore we assign *a* to these fluorines at position 1". The fluorines at position 2' would likely yield the most shielded trifluoromethyl resonance because they are near the trimethyl silane substituent. So we assign the pair of triplets, *f*, located at -81.4 ppm, to this trifluoromethyl group. Since this trifluoromethyl group is next to a chiral center, there is a possibility that we are observing a set of enantiomers. We assign the tall unresolved resonance, *c*, at -79.8 ppm to the remaining CF₃ labeled 3.

The small peak at -84.2 ppm is due to an impurity. We expect the difluoromethylene at position 2" in the propoxy group to absorb where we find peak *g*, at -129.7 ppm. This peak forms the inner part of an AB pattern where the two outer legs are less than 1% of the two central legs that are almost coincident.

We must now assign the multiplets *h* and *i*, at -145.1 ppm and -148.0 ppm. Since *i* is the most shielded resonance, we assign it to the fluoromethine group at position 1' of the ethoxy group, directly bonded to the trimethylsilyl group. The remaining resonance at -145.1 ppm, *h*, is assigned to the fluoromethine group at position 2 in the propane chain. Moreover, the location of peak *h* is consistent with our experience for the chemical shift of this type of fluorinated substituent.

2,4,6-Tris[perfluoro-1-[perfluoro-2-(perfluoropropoxy) propoxy] ethyl]-1,3,5-triazine (XVI). A sharp impurity peak at -88.5 ppm is obvious in the 470 MHz one-dimensional spectrum for this molecule shown in Figure 2-28. As in the case of compound XII, the trimethylsilyl mono-ether, and compound XIV, the triazine mono-ether above, the terminal trifluoromethyl group for this di-ether moiety moves upfield slightly after a triazine ring is substituted for the corresponding trimethylsilyl group. A very complicated multiplet, *a*, is found at -78.8 ppm that has an area consistent with two fluorine nuclei in this spectrum. The area for this peak together with its chemical shift indicates that *a* is one of the two oxydifluoromethylene groups in the molecule.



We observe two singlets, *b*, at -80.5 ppm that overlap an unresolved multiplet. From its chemical shift and area, we assign *b* to a trifluoromethyl group. At -81.7 ppm we observe another broad singlet, *d*, overlapping an unresolved multiplet centered at -81.4 ppm, where there may also be some indication of the molecule degrading. Nonetheless, the total area of the peaks around *c* and *d* is indicative of two trifluoromethyl groups and an oxydifluoromethylene group.

There is a tall peak, *e*, at -129.9 ppm whose area and chemical shift is consistent with what we expect for the difluoromethylene group at position 2". There are two sets of overlapping multiplets at -132.9 ppm, *f*, and at -144.6 ppm, *g*. The area for each of these multiplets is consistent with that of a single fluorine nucleus. Moreover, we can assign the most deshielded of the two multiplets, *g*, to the fluorine nucleus at position 1' adjacent to the triazine ring. Therefore peak *f* is assigned to the fluorine nucleus at position 2 in the propane substituent.

To make further assignments, we use the correlation spectrum shown in Figure 2-29. Although the peaks between -78.0 and -82.0 ppm are not resolved well in the two-dimensional spectrum, we can see that the multiplet *a* is coupled to peaks *b* and *f*. Since we previously assigned *f* to position 2 in the propane substituent, we can assign *a* to the oxydifluoromethylene group at position 1" in the propoxy substituent. Placing *a* at position 1" enables us to assign peak *b* to position 3", the terminal trifluoromethyl group in the propoxy substituent. Furthermore, the multiplet *c* is assigned to position 1, the

Figure 2-28. One-Dimensional Spectrum of Compound XVI

2,4,6-Tris[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-1,3,5-triazine

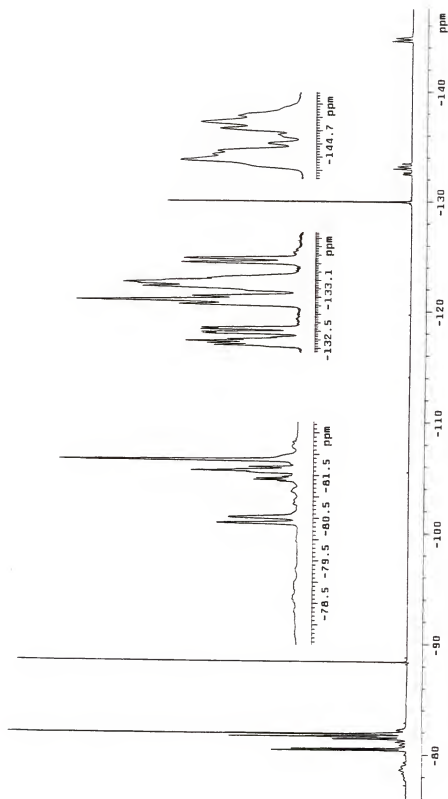


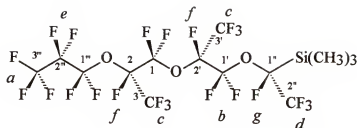
Figure 2-29. Two-Dimensional Spectrum of Compound XVI
2,4,6-Tris[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-1,3,5-triazine

difluoromethylene substituent in the propane group by default. This assignment is confirmed by the correlation peak between *c* and *f* in Figure 2-29.

Peak *f* is also coupled to *d* and to peak *g*. Thus the trifluoromethyl groups at positions 3 and 2' have the same chemical shifts. So we assign *d* to the trifluoromethyl groups at these positions. Moreover, it appears that the corresponding fluoromethine group labeled *f* in the precursor molecule, has shifted from -144.6 ppm to -132.9 ppm in this molecule. Finally we see a weak correlation between peaks *d* and *e*. This represents a six-bond coupling between the fluorine nuclei at positions 2'' and 3.

It is noteworthy that we observe that there are two peaks *b*, *f*, and *g* in the spectrum of this molecule while there exists one in the spectrum of, compound XV, the molecule without the triazine substituent. Because there are two chiral centers in this molecule--one at position 1 on the ethoxy substituent and another at the number 2 position of the propane chain--we might speculate that the chemical shifts of peaks *f*, *g* are slightly different in each of the enantiomers. It is also likely that more than one conformation for the polyether substituents is energetically accessible. Either one or both of the aforementioned phenomena are sufficient cause to observe more than one spectrum. Furthermore, the peak *f* is shifted downfield from the corresponding peak in compound XV by approximately twelve ppm in the spectrum of the triazine.

Perfluoro-2,2-dimethyl-3,6,9-tris(trifluoromethyl)-4,7,10-trioxa-2-silatridecane (XVII). This molecule has one more OCF₂CF(CF₃) repeating unit than does compound XV. This monomer unit introduces another chiral center as well as another oxydifluoromethylene group. Consequently, more transitions appear to be doubled and one more non-first order pattern is introduced into the spectrum. Figure 2-30 shows the one-dimensional spectrum for this molecule. As in Figures 2-27 and 2-28, the non-first order patterns overlap with the fluoromethyl transitions at -78.8, -80.7, and -82.2 ppm.



XVII

In compounds XIII and XV, molecules bearing the trimethylsilyl substituent, we found the terminal fluoromethyl group near -78.0 ppm. In the spectrum of this molecule, there are two doublets, designated *a*, at -78.8 ppm. There are also two multiplets, possibly pentets, for the resonance designated *c* at -80.7 ppm. The area of *c* is twice the area of *a* so we assign it to the two trifluoromethyl groups bonded to the two fluoromethine groups in the middle of the chain. The area of the pair of overlapping singlets, *d*, at -82.2 ppm is not a multiple of the previous two because it includes more of a coincident non-first order pattern than do the peaks *a* and *c*. Nonetheless its area is considerably less than what one would expect for two fluoromethyl groups but close to the area for one trifluoromethyl group. Thus *d* is assigned to the trifluoromethyl group nearest to the trimethylsilyl group.

The COSY spectrum of this molecule is not shown here. Nevertheless this spectrum indicates a crosspeak between the non-first order pattern, *b*, that is coincident with *a*, and the pair of quartets far upfield at -149.6 ppm, designated *g*. From our previous experience with the chemical shift of these molecules we assign the quartets, *g*, to the fluoromethine unit bonded directly to the trimethylsilyl group.

The correlation spectrum shows that the trifluoromethyl group, *d*, is also coupled with this fluoromethine group. This observation confirms the assignment for *d* above: *d* is the trifluoromethyl group closest to the trimethylsilyl group. The two overlapping multiplets at -145.5 ppm, *f*, has twice the area of *g* and are correlated with the pair of overlapping multiplets, *c*, at -80.7 ppm. We therefore assign *f* to the two fluoromethine groups in the middle of the chain and assign *c* to the two respective trifluoromethyl groups

Figure 2-30. One-Dimensional Spectrum of Compound XVII

3,5,5,6,8,8,9,11,11,12,12,13,13-Tetradecafluoro-2,2-dimethyl-3,6,9-tris(trifluoromethyl)-4,7,10-trioxa-2-silatridecane

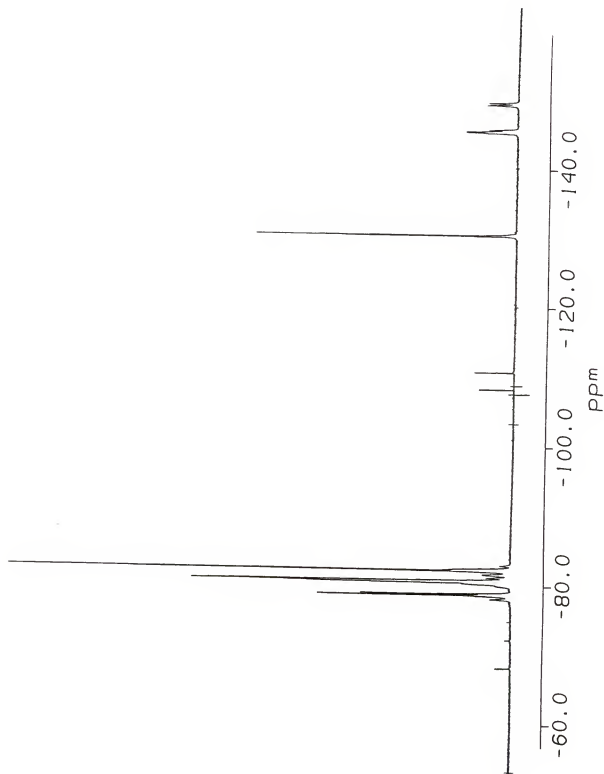


Figure 2-31. One-Dimensional Spectrum of Compound XVIII
2,4,6-Tris[1,2,2,2-tetrafluoro-1-[1,1,2,3,3-hexafluoro-1-[1,1,2,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-1,3,5-triazine

Figure 2-32. DQFCOSY Spectrum of Compound XVIII
2,4,6-Tris[1,2,2,2-tetrafluoro-1-[1,1,2,3,3-hexafluoro-1-[1,1,2,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-1,3,5-triazine

areas and because we expect the chemical shift of trifluoromethyl group and oxydifluoromethylene units to be nearly coincident, we conclude that the transitions *b* and *c* each represent two trifluoromethyl groups. The remaining oxydifluoromethylene substituents are responsible for the multiplets *b'* and *c'*.

We observe a tall unresolved resonance, *d*, at -130.4 ppm. Peak *d* has an area indicative of two fluorine nuclei. Moreover it is located where we expect to find the difluoromethylene unit bonded directly to the terminal trifluoromethyl group.

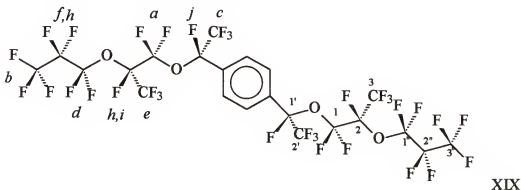
The multiplet at -133.3 ppm is labeled *e*. The relative area for this transition represents one fluorine nucleus. We come across two more overlapping multiplets at -145.3 ppm. We label these transitions *f* and note that their area indicates two fluorine nuclei. We assign *e* and *f* to the fluoromethine groups in the molecule. We might expect the fluoromethine unit bonded directly to the triazine ring to have a chemical shift significantly different from the other two fluoromethine groups in the molecule. Therefore we assign *e* to the unique fluoromethine unit and *f* is assigned to the fluoromethine units in the middle of the chain.

In Figure 2-32, the two-dimensional correlation spectrum of this molecule, we observe several correlation peaks that confirm our assignments. The multiplet *a* is coupled to *e*. So we assign *a* to the CF₂O group at position 1'. Peak *b* is coupled to *f*, and this enables us to assign *b* to the trifluoromethyl group at position 3. The area of *b* is indicative of another trifluoromethyl group. Since the location of *b* is consistent with that of terminal trifluoromethyl group, we assign *b* to position 3'''. So the resonances from the trimethyl groups at positions 3 and 3''' Peak *c* is coupled to peaks *d*, *e*, and *f*. Therefore we assign *c* to the trifluoromethyl groups at positions 2'' and 3'. The multiplet *c'* is coupled to *f*, so we assign this resonance to the difluoromethylene group at position 1. Thus the multiplet *b'* is assigned to the remaining CF₂O group at position 1'''.

1,4-Bis[tetrafluoro-1-[hexafluoro-2-(heptafluoropropoxy) propoxy] ethyl] benzene (XIX). The fluoro-diether substituents found in compounds XV and XVI are

symmetrically placed on a phenyl ring in this molecule. This provides us the opportunity to observe electronic effects produced by the phenyl ring by comparing these spectra.

As in the previous molecules, several complicated non-first order multiplets, indicative of the oxydifluoromethylenes, are evident in the spectrum shown in Figure 2-33. An expanded view of the correlation spectrum, shown in Figure 2-34, reveals that there are at least two overlapping non-first order patterns between -79.0 and -83.0 ppm. Much of the non-first order patterns clutters the spectrum around the partially resolved triplets, *b* and *c*, located at -80.5 and -81.5 ppm. We cannot assign these multiplets uniquely, because of this severe overlap. However for the purposes of this discussion, we shall associate the multiplets around -79.2 and -82.2 ppm with the letters *a* and *d*. Moreover, it is also likely that the non-first order patterns are coupled to each of the more intense peaks *b*, *c*, and *e* that indicate trifluoromethyl groups.



XIX

In Figure 2-33, it is evident that the peaks *b*, at -80.5 ppm, and *c*, at -81.5 are partially resolved triplets. We expect that the chiral centers will influence the chemical shifts of the enantiomers, but we do not try to distinguish between the two. Therefore we label the overlapping pair of doublets, at -84.1 and -84.2 ppm, as one unit, *e*. There are two overlapping singlets at -129.4 ppm that we label *f*, and another intense singlet at -129.5 ppm labeled *g*. As in the previous molecules, we assign these peaks to the difluoromethylene unit at position 2" in the fluoropropane chain. This group is

Figure 2-33. One-Dimensional Spectrum of Compound XIX

1,4-Bis[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]benzene

FILE: #8888-23
 UNITYplus-500 "csmnar1"
 PULSE SEQUENCE
 Delay 1.500 sec
 Pulse 63.0 degree
 Acq. time 2.580 sec
 Width 48513.7 Hz
 32
 OBSERVE F19, 476.321282 MHz
 DATA PROCESSING
 F19, 476.321282 MHz
 Total time 2 minutes

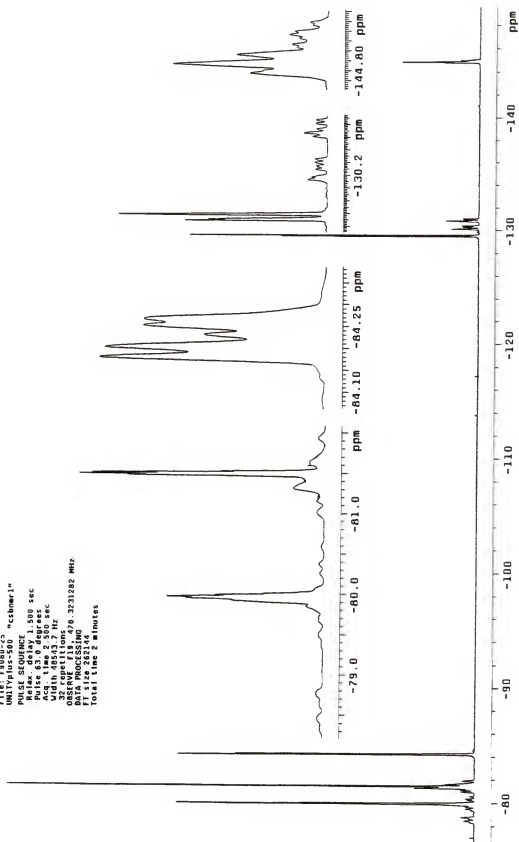


Figure 2-34. Expanded DQFCOSY Spectrum of Compound XIX

1,4-Bis[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]benzene

Figure 2-35. DQFCOSY Spectrum of Compound XIX

1,4-Bis[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]benzene

represented by more than one peak because the molecule is chiral and possibly because of distinct conformations available to this molecule. Both *e* and *f* have relative areas indicative of two fluorine nuclei.

We find a multiplet at -130.2 ppm that we label *h* and triplets at -130.8 and -144.8 ppm that we label *i* and *j* respectively. Peaks *h*, *i*, and *j*, have relative areas which indicate one fluorine nucleus each. Their chemical shift and relative areas suggest that these peaks are representative of fluoromethine fluorines. Because *j* is the most deshielded resonance, we assign it to the fluoromethine unit directly bonded to the phenyl ring.

Figure 2-35 is the entire two-dimensional correlation spectrum of this molecule. It enables us to assign these resonances with more certainty. The fluorine nucleus, *j*, is coupled to *c*, and perhaps also coupled to the cluster of peaks around this trifluoromethyl group. Consequently, we assign *c* to the trifluoromethyl group at position 1 in the chain.

The fluorine nuclei represented by *h* and *i* are coupled to the two overlapping doublets at *e*, which represents a trifluoromethyl group. Correlating these two peaks enables us to assign *e* to the trifluoromethyl group at position 4 in the di-ether chain. Furthermore, it is likely that *h* and *i* belong to distinct enantiomers or to distinct conformers, consistent with the fact that there exist a superposition of the overlapping doublets at *e*.

Part of the non first-order pattern that we designated as *a* is coupled to the fluorine nucleus represented by *i* downfield at -130.8 ppm. Since *a* and *e* couple, we may associate the oxydifluoromethylene unit represented by *a* with the two fluorine nuclei at position 1 in the chain.

The terminal trifluoromethyl group is then assigned to the triplet, *b*, at -80.5 ppm. Since we have previously assigned part of the AB pattern designated *a*, we can assign the non-first order pattern centered at -82.1 ppm to the fluorine nuclei at position 6.

Perfluoro-2-[hexafluoro-2-(heptafluoropropoxy)propoxy]-1-pentafluorophenyl)-1-propanone (XX). The perfluoro-diether substituent found in compounds XV, XVI,

and XIX is bonded to a pentafluorobenzoyl group in this molecule. The spectrum of this molecule, shown in Figure 2-36, is complicated by the presence of a number of impurity peaks: a triplet at -75.4 ppm, a multiplet at -135.3 ppm, and another triplet at -164.0 ppm. The impurity at -75.4 ppm is especially troublesome as it coincides with the non-first order patterns indicative of the oxydifluoromethylene groups that have been especially difficult to analyze. Nonetheless, there are two non-first order multiplets between -77.0 and -82.0 ppm in the one-dimensional spectrum. Figure 2-37 is an expanded view of the two-dimensional correlation spectrum. Upon examining it we see that two overlapping AB patterns are evident. We come across the first AB pattern at -77.6 and -81 ppm and label it *af*. These doublets are coupled by 141.1 Hz. The doublets *b* and *d*, the second AB pattern, located immediately downfield at -78.1 and -80.6 ppm are coupled by approximately 148 Hz. Without the resolving power of the t_1 dimension, it is doubtful that we would identify the connectivity of these multiplets.

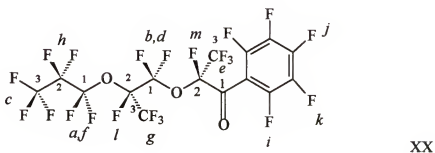


Figure 2-36 displays three singlets where we expect to find the trifluoromethyl groups at -80.3, -80.6, and -81.66 designated *c*, *e*, and *g*. Peak *c* is a pair of unresolved, overlapping singlets, and peaks *e* and *g* are relatively broad.

An unresolved doublet or another pair of overlapping singlets, designated *h*, is located at -129.0 ppm. Both the chemical shift and the relative area indicate that *h* is the difluoromethylene unit at position 8 in the chain.

Figure 2-36. One-Dimensional Spectrum of Compound XX

2,3,3,3-Tetrafluoro-2-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]-1-(pentafluorophenyl)-1-propanone

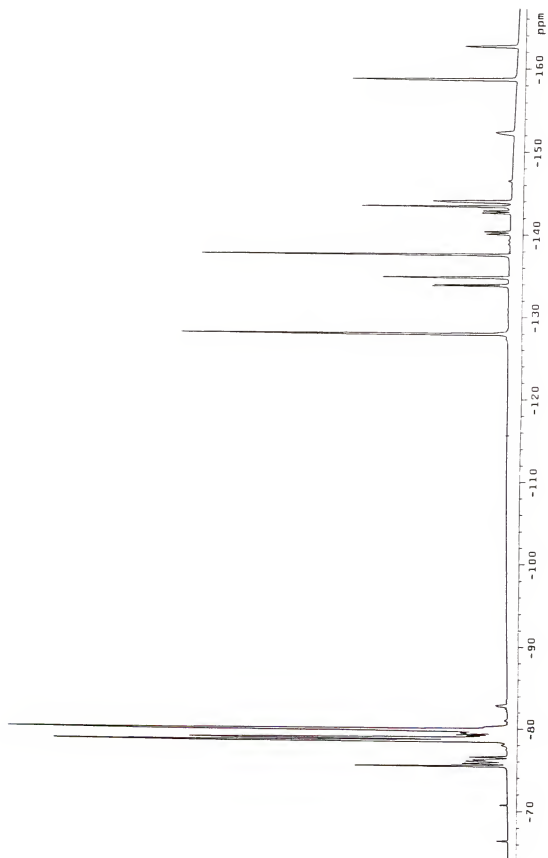
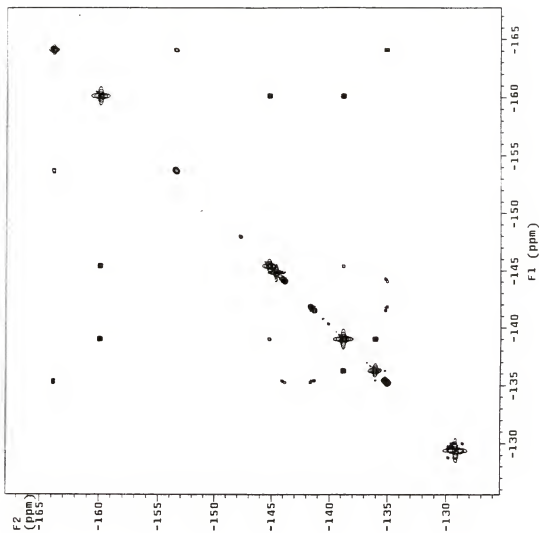


Figure 2-37. Expanded Spectrum of Compound XX

2,3,3,3-Tetrafluoro-2-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]-1-(pentafluorophenyl)-1-propanone

SAMPLED Jul 28 93 DEC. & VT
 date Jul 28 93 dn f18
 solvent /acetone- d6f
 f18018-ccyav dar
 nar1/west/sep/1018-
 /1018-ccyav dar
 200
 ACQUISITION 25.0
 sfrq 470.268 temp
 tn 0 f18
 t 16384 sb
 m 16384 sb
 sw 48543.7 wf file not used
 lb 26700 proc fl
 ss 32 math 8192
 tprw 57
 pw 7.0 werr
 pl 5.000 wcp
 dl 5.000 wcp
 phase -3231.0 unit
 nt 16 sb
 cl 16 sb not used
 clock 16 sb
 gain 0 proc
 ll flags n sb
 in n sp display 8192
 dp y up 78953.4
 h 20 ACQUISITION 500
 sw1 48543.7 wc 145
 nt 20 DISPLAY 512 hzmm 394.76
 sp1 -78993.3 rfi 45402.3
 wp1 19820.5 rfp -33858.3
 wc2 145 line 1.000
 rfi1 45402.3 al av
 rfp1 -33858.3



Two multiplets are found at -136.3 and -139.1 ppm that we label *j* and *k*. The relative area of *j* represents a single fluorine nucleus and the relative area for *k* is twice that of *j*. From the chemical shifts and the relative areas, we assign *j* to the fluorine nucleus at the para position, and *k* to the two fluorine nuclei at the ortho position, in the perfluorophenyl ring.

Two triplets designated *l* and *m* are found at -145.1 and -145.7 respectively. Both the relative areas and chemical shifts of these nuclei suggest that they represent the fluoromethine units in this molecule. The remaining triplet at -160.4 ppm that we label *n* has a relative area and chemical shift indicative of the two fluorine nuclei at meta positions in the phenyl ring.

The entire COSY spectrum of this molecule is shown in Figure 2-38 and it reveals some interesting correlations. A crosspeak exists between the AB pattern designated *af* and the trifluoromethyl fluorines, *c*. Since *c* does not appear to be coupled to a fluoromethine group, we shall assign *c* to the terminal CF₃ group. Consequently, the oxydifluoromethylene group represented by *af* is likely to be located beta to *c*.

The *a* nucleus in this oxydifluoromethylene group appears to be further coupled to the CF₃ fluorines in *g*. Thus we expect that *g* is located on the fluoromethine unit at position 7 in the di-ether chain. We see another crosspeak between *g* and one of the fluoromethine fluorines, *l* or *m*. Though the correlation peaks for *l* and *m* overlap in the region around *g* and *c*, we shall assign the triplet *l* to the fluoromethine unit at position 7. Peak *l* is located at higher field of *m*. Moreover, *m* is surprisingly coupled through six bonds to the aromatic fluorines, *n*, at the meta position of the ring.

The other AB pattern, *bd*, must be assigned to the remaining oxydifluoromethylene group at position 4 of the chain. We see that *g* is also coupled to nucleus *b*, which is consistent with the assignments above. The correlation spectrum further shows the coupling between the aromatic fluorines at the para and the meta positions.

Figure 2-38. COSY Spectrum of Compound XX

2,3,3,3-Tetrafluoro-2-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]-1- (pentafluorophenyl)-1-propanone

The trifluoromethyl group e appears to couple with m , the neighboring fluorine nucleus at position 2. Surprisingly e clearly couples to the ortho aromatic fluorines, k . Like nuclei m and n , nuclei e and k couple over six bonds. We shall see later that a carbonyl oxygen can facilitate long range coupling. Moreover, there is a possibility for the carbonyl group and the aromatic ring to cooperate in transmitting these nuclear spin-spin couplings.

CHAPTER 3 CARBON-13-FLUORINE-19 NMR SPECTROSCOPY

One-Dimensional Carbon-13 NMR

Less is known about carbon-fluorine indirect nuclear coupling than is known about either carbon-hydrogen J couplings or fluorine-fluorine J couplings. To learn how carbon-fluorine J couplings vary with chemical substituents, we acquired the fully coupled carbon spectra of a number of fluorocarbons. The low natural abundance and relatively small magnetogyric ratio of the carbon-13 nucleus make this nucleus relatively insensitive. The signal-to-noise ratio can be improved by simply summing the free induction decay from thousands of acquisitions. Furthermore, the longitudinal relaxation time for the carbon nucleus is often more than twice as long as the corresponding relaxation time for the fluorine nucleus. So we commonly use an Ernst angle⁵⁷ to recover the magnetization more efficiently. Nonetheless, before a new transient begins, one typically must wait a longer time than one does when acquiring fluorine.

Direct interpretation of these carbon-13 spectra is also complicated by severe overlap of the resonances because many of the carbon resonances occur in the same area of the spectrum. Interpretation of the spectra is facilitated by decoupling the carbon-13 spectrum and comparing the decoupled spectrum with the corresponding coupled carbon-13 spectra. A method, that is straightforward in principle, for simplifying carbon-13 spectra is to irradiate the entire spectrum of the more receptive nucleus while one acquires the carbon-13 free induction decay: a technique known as broadband decoupling. A requirement of good broadband decoupling is that the irradiation power be sufficient throughout the spectrum of the irradiated nucleus.

With one of the earliest methods of broadband decoupling, called noise modulation, one randomly modulates the decoupler frequency⁵⁸. To decouple a spectral width of 5 kHz using 600 Hz noise modulation, one typically uses a moderate decoupling power of about 10 watts. By reducing the overlap of the multiplets noise decoupling simplifies the spectrum and improves the signal-to-noise ratio in the spectrum because each carbon signal is concentrated into a singlet.

In one version of gated double resonance, the abundant nucleus is irradiated with low power as the carbon magnetization is allowed to recover between acquisitions. The relative populations of the carbon nuclear energy levels are distributed according to the nuclear Overhauser effect, providing as much as a twofold increase in signal intensity.⁵⁹ During the acquisition period, the decoupler power is increased to provide a decoupled spectrum. Using noise modulation, one can adequately decouple all proton-carbon heteronuclear couplings, but this method cannot achieve sufficient decoupling power throughout the wider fluorine spectral width.

Modern spectrometers use broadband decoupling sequences that achieve the objectives above with even less power. The decoupling sequence most commonly used is called WALTZ.^{60,61,62} Many spectrometers are designed with a specific chip that provides ability to define the phase shifts and pulse lengths necessary to perform this sequence.

Broadband decoupling sequences allow one to decouple nuclei with a 20 kHz spectral width with no more power than is used to decouple a 5 kHz spectral width using noise modulation. To decouple fluorine, the hardware of the NMR spectrometer must have a transmitter on the decoupler channel capable of generating the fluorine decoupling frequency and a pulse programmer capable of achieving the decoupling sequences. The increased use of indirect detection experiments^{63,64} has inspired a generation of commercial spectrometers equipped with flexible pulse programmers, and circuitry that switches between two or more frequency channels, each possessing a separate broadband transmitter. Furthermore, the design of the indirect detection probe places the high band

radio frequency coil closer to the sample, providing the user with an even larger decoupling band width.

We acquired the decoupled carbon spectra presented in this section using the gated decoupler technique combined with the decoupling sequence called GARP-1.⁶⁵ Even with these methods, we found it necessary to use rather high decoupling transmitter power.

Heteronuclear Multiple Quantum Coherence Spectroscopy

To correctly assign the carbon spectrum, it became necessary to correlate carbon resonances with the previously assigned fluorine spectrum. The preferred method for correlating these resonances is to use the two-dimensional indirect-detection experiment. With this method we detect the chemical shift of fluorine in the t_2 dimension, and detect the chemical shift of carbon to which it is directly bonded in the t_1 dimension. The signal-to-noise ratio improves using this method as compared with detecting the less receptive carbon-13 nucleus directly. Martin has reviewed several versions of the indirect detected heteronuclear multiple quantum coherence (HMQC) experiments,^{66,67} but not many fluorine-detected heteronuclear correlation experiments have been reported.⁶⁸

Even with a spectrometer designed for indirect detection, one must avoid or suppress the strong signals from the abundant nuclei that are not coupled to the rare nucleus. Bax and coworkers avoided the dynamic range problem with a difference experiment.⁶⁹ The basic pulse sequence is shown in Figure 3-1. This sequence avoids signals from the fluorine nuclei attached to carbon-12 by alternating the phase of the receiver and the first pulse on the carbon channel together on successive acquisitions. Consequently, signals from the fluorines attached to carbon-13 nuclei have the same phase as the receiver for each scan, while signals from the fluorines attached to carbon-12 have a phase opposite that of the receiver for every other scan. With signal averaging, the

fluorine resonances attached to carbon-13 are reinforced and those fluorines attached to carbon-12 cancel.

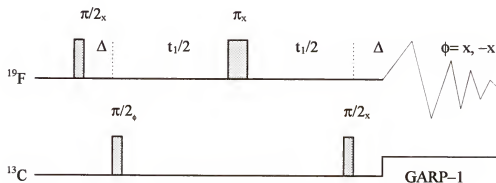


Figure 3-1
Basic Heteronuclear Multiple Quantum Coherence (HMQC) Pulse Sequence

The initial $\pi/2$ high-band pulse places the fluorine magnetization in the transverse plane where it evolves with its chemical shift and coupling constant. The time Δ is set to $1/(2J_{CF})$ during which we expect the two components of the fluorine doublet to dephase. The first $\pi/2$ pulse on the carbon-13 band converts all the transverse fluorine magnetization into heteronuclear zero- and double-quantum coherence.

The π pulse on the high-band channel interchanges the zero- and double-quantum coherences at the midpoint in the evolution. Interchanging the coherence levels allows us to detect resonances centered at $(F_1, F_2) = (\pm\delta^{13}\text{C}, \delta F)$: there is a direct correlation between the two dimensions. If we remove this π pulse, the carbon chemical shift would have a contribution from the chemical shift of the abundant nucleus.

A final $\pi/2$ pulse converts the multiple-quantum coherences into ^{19}F transverse magnetization. The two components of the fluorine doublet are in antiphase immediately after this pulse. Decoupling the rare nucleus at this point would cancel our signal. We can, however, decouple the carbon nucleus after waiting a period $\Delta = 1/(2J_{CF})$.

Bax and Subramanian⁷⁰ improved upon this indirect detection method by placing the bilinear rotation decoupling (BIRD)⁷¹ pulse cascade in front of the basic HMQC sequence. The BIRD pulse cascade is shown in Figure 3-2. It acts as a π pulse for the abundant nuclei that are not directly coupled with the rare nuclei, and acts as a 0° pulse for

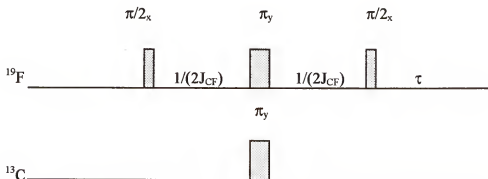


Figure 3-2
Bilinear Rotation Decoupling Pulse Sequence

those fluorines that are directly coupled with carbon-13 nuclei. We start the first $\pi/2$ pulse of the HMQC sequence after waiting a time τ after the BIRD pulse until the magnetization for most of the fluorines attached to carbon-12 has recovered to the transverse plane through relaxation processes. Hence this modification suppresses the unwanted fluorine resonances more effectively than the basic HMQC sequence.

Experimental

Spectra were collected on a Varian Unity 500 NMR spectrometer operating at 11 tesla, or a Nicolet-GE-Bruker NT-300 spectrometer operating at 7 tesla. A coupled carbon-13 spectrum was obtained on the Unity 500 using a lower decoupling power level during the recovery period to provide a NOE buildup that improved the sensitivity. Bilevel decoupling was used to acquire decoupled carbon spectra for all molecules except for 1-[2,3,4,5,6-pentafluorophenyl]-1,3,3,3-tetrachloro-1,2,2-trifluoropropane. For this

molecule, we used a constant decoupling power. Broadband decoupling was achieved using the GARP-1 decoupling sequence. A 6 microsecond fluorine 90° pulse width and a 13.5 microsecond carbon 90° pulse width were used in the HMQC experiments. A set of trial BIRD sequences were performed to determine the optimum null time for each molecule. During collection of all these spectra, precooled nitrogen gas was passed through the probe so that the sample did not overheat.

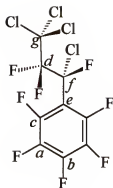
Discussion and Results

1-[2,3,4,5,6-Pentafluorophenyl]-1,3,3,3-tetrachloro-1,2,2-trifluoropropane (XXI)

The one-dimensional carbon-13 spectrum is shown in Figure 3-3. The aromatic carbons are located between 136.0 and 148.0 ppm and are large doublets, each of which contains further splitting. The resonance at 143.5 ppm, *b*, has about half the area of either *a*, centered at 145.3 ppm, or *c*, centered at 138.4 ppm. Therefore, we assign *b* to the carbon at the para position in the perfluorophenyl ring.

Although the fluorine 1-D and heteronuclear correlation spectra for this molecule are not shown, they confirm that peak *a* and peak *c* are due to the meta and ortho carbons respectively. Peak *a* is correlated to the aromatic fluorine at -159.5 ppm and peak *c* is correlated to the aromatic fluorine at -130.3 ppm. The fluorine peak at -159.5 is a triplet of doublets and the fluorine peak at -130.3 ppm is a very broad singlet. Assigning the fluorine peak at lower frequency to the meta fluorines is consistent with chemical shift and multiplicity of this resonance. The chemical shift of the broad singlet at higher frequency is consistent with the location of the ortho fluorine atoms.

The remaining aromatic resonance is the unresolved multiplet at 110.5 ppm, and we assign it to the number 1 carbon atom on the phenyl ring. This is a complicated multiplet because it is coupled through three or more bonds to several fluorine nuclei in the aromatic ring and in the aliphatic side chain.



XXI

Peak *a* appears to be a doublet of doublets of doublets centered at 145.3 ppm. The fluorine nuclei bonded directly to these carbon atoms cause a splitting of 261.4 Hz. The fluorine at the adjoining position causes a doubling of 9.0 Hz. Finally there is a smaller 4.1 Hz that is most likely a three-bond coupling from the other meta fluorine nucleus.

The multiplet *c* appears to be a doublet of triplets of triplets, but in fact it is a doublet of doublets of doublets of doublets. The doubling 253.7 Hz wide is due to coupling from the fluorine nucleus directly bonded to the ortho carbons. This is the smallest one-bond bond coupling constant found in this study, and its magnitude may reflect an electronic effect from the chlorofluoropropyl substituent. The 12.4 Hz splitting is due to the two-bond coupling from the fluorines at the meta position. The smaller doublets overlap a great deal, and this overlapping splitting appears to be a triplet in the carbon-13 spectrum that arises from the coupling to the other ortho and para fluorine atoms in this molecule. Thus the reported magnitudes for $^3J_{CF}$ in Table 3-1 are average values.

The multiplet from the para carbon, *b*, is a doublet of triplet of triplets. The large doubling of 261.2 Hz is due to the single fluorine atom to which it is directly bonded. The

Figure 3-3. Coupled Carbon-13 Spectrum of Compound XXI
1,1,1,3-Tetrachloro-2,2,3-trifluoropropyl-2,3,4,5,6-pentafluorobenzene

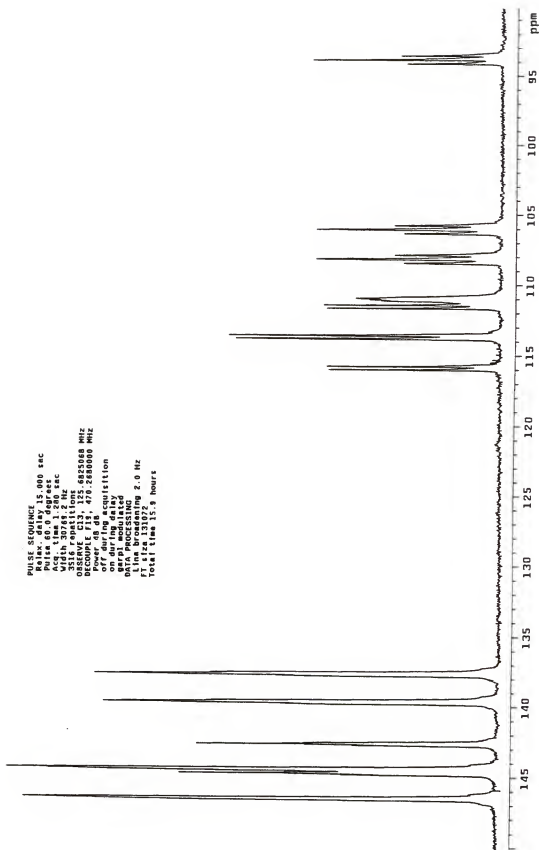
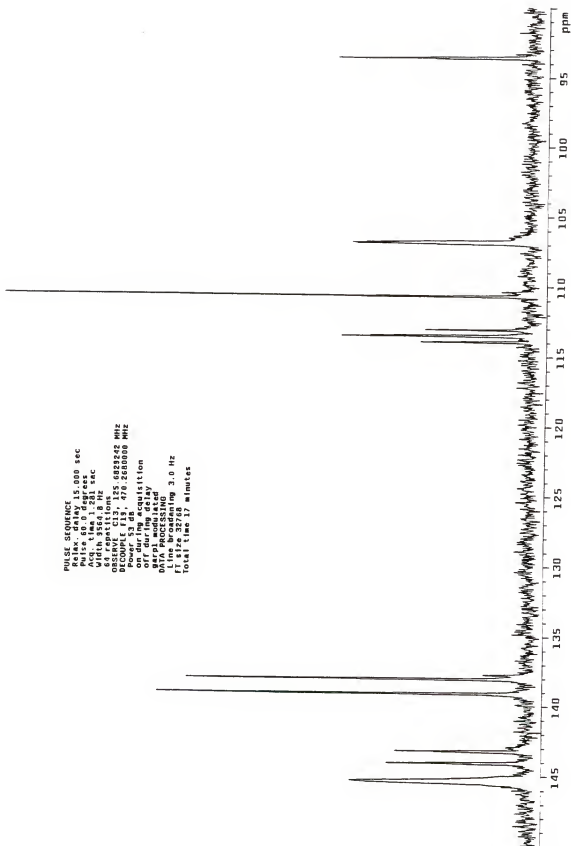


Figure 3-4. Decoupled Carbon-13 Spectrum of Compound XXI
1,1,1,3-Tetrachloro-2,2,3-trifluoropropyl-2,3,4,5,6-pentafluorobenzene

PULSE SEQUENCE
 Pulse program 15.080 sec
 Pulse 50.0 degrees
 Acq. time 1.281 sec
 Nucleus 13C, 125 MHz
 66 repetitions
 OBSERVE C13, 125.6823242 MHz
 DECOUPLE 13C, 125.6823242 MHz
 Power 53.88, 476.2680000 MHz
 on during acquisition
 off during delay
 DATA PROCESSING
 Line broadening 3.0 Hz
 Frequency offset 0.000000
 Total time 17 minutes



larger triplet of 13.2 Hz is due to the two-bond coupling from the two meta fluorines on the phenyl ring, and the smaller tripling of 4.1 Hz is a three-bond coupling from the two ortho fluorines. It is worth noting that in hydrogenated aromatic compounds, the two-bond carbon-hydrogen coupling is smaller than the three-bond carbon-hydrogen coupling. Furthermore, the average two-bond carbon-fluorine coupling is 21.0 Hz in perfluorinated benzenes⁷² but in this compound the average two-bond coupling is 11.5 Hz.

The number 2 carbon atom in the propane chain is assigned to the triplet of doublets, *d*, at 113.5 ppm. We assign the doublet of triplets at 106.7 ppm, *f*, to the number 1 carbon atom of the propane chain, and we assign the triplet with the small splitting at 93.4 ppm, *g*, to the third carbon atom of the propyl chain.

Table 3-1

Carbon Nucleus	Chem. Shift (ppm)	$^1J_{CF}$ (Hz)	$^2J_{CF}$ (Hz)	$^3J_{CF}$ (Hz)
<i>a</i>	145.2	261.4	9.0	4.1
<i>b</i>	143.5	261.2	13.1	4.7
<i>c</i>	138.4	253.7	12.4	4.5
<i>d</i>	113.4	273.3	28.7	
<i>e</i>	110.5			
<i>f</i>	106.7	264.6	36.0	
<i>g</i>	93.4		35.7	

There is a 27 kHz fluorine spectral width for this molecule. Figure 3-4 shows an unsuccessful attempt to decouple this spectrum. Although the decoupler frequency was modulated with the GARP-1 pulse cascade, the power level for broadband decoupling was not sufficient. There is still a considerable amount of residual coupling for peaks *b*, *c*, and *e*. The two-bond coupling is removed from each peak in the spectrum but the one-bond coupling, which is eleven times larger than the average two-bond coupling, is only reduced in magnitude. The one-bond coupling in this molecule ranges from 253.7 to 273.3 Hz,

while the corresponding two-bond coupling ranges from 13.3 to 36.0 Hz. The specific coupling constants associated with each nucleus are summarized in Table 3-1.

1,2,2-Trichloroperfluoro-octane (V). Figure 3-5 illustrates the complexity that one may expect in a fluorine-coupled carbon spectrum. We can easily see the intense triplet at 127.0 ppm that displays a 301.7 Hz one bond coupling constant. We assign it to the number 1 carbon in the perfluoroalkane chain, and labeled it *a*. A small pentet located at 85.2 ppm, which is not shown in the Figure, is assigned to the number 2 carbon, *h*. The eighth carbon atom, *b*, is assigned to the quartet of triplets centered at 117.9 ppm. The one- and two-bond coupling constants for this carbon atom are 287.8 and 33.1 Hz respectively. However it is difficult to make any further assignments in this spectrum.

The decoupled carbon spectrum of this molecule is shown in Figure 3-6. It is obvious that a bilevel decoupling using GARP-1 modulation can cleanly remove J coupling over 31.5 kHz, the fluorine spectral width for this molecule. However, it is necessary to use the heteronuclear correlation spectrum, shown in Figure 3-7, to make the carbon peak assignments.



V

Because peak *b* is relatively intense in the fluorine spectrum of this molecule, a streak across f_1 appears where $f_2 = -81$ ppm. Nevertheless, it is now possible to assign peaks *c*, *d*, *e*, *f*, and *g* respectively to the third, fourth, fifth, sixth, and seventh carbon atoms in the octane chain. It is noteworthy that the order of assignments in the carbon spectrum is similar to that found in the fluorine spectrum.

One can now overlay the coupled and decoupled spectra to learn the center of individual resonances and figure out their respective multiplicities. Peaks *f*, *e*, and *d* are

Figure 3-5. Coupled Carbon-13 Spectrum of Compound V
1,2,2-Trichloroperfluorooctane

Temp 25.0 C / 298.1 K
 User : 08-14-87
 UNITplus-500 -cctbmr1=
 PULSE SEQUENCE
 Relax delay 15.000 sec
 Acq time 1.0000000000000000
 Acq time 1.0000000000000000
 Width 30768.2 Hz
 2560 repetitions 6824534 MHz
 OBSERVE F1 - 470.2560000 MHz
 Power 48 dB
 on during acquisition
 garpi modulated
 antenna matching
 Line frequency 2.0 Hz
 FF size 131072
 Total time 13.0 hours

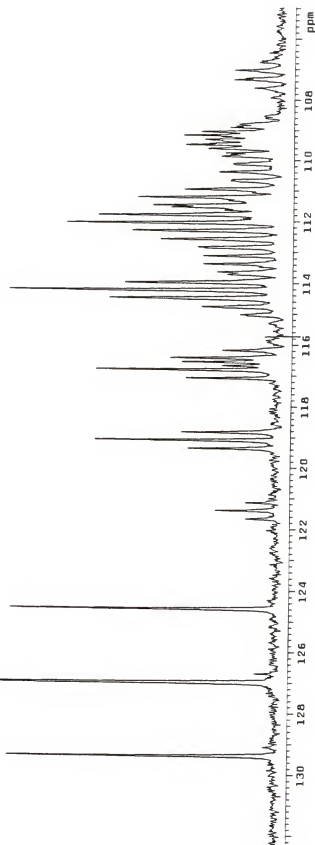


Figure 3-6. Coupled Carbon-13 Spectrum of Compound V
1,2,2-Trichloroperfluorooctane

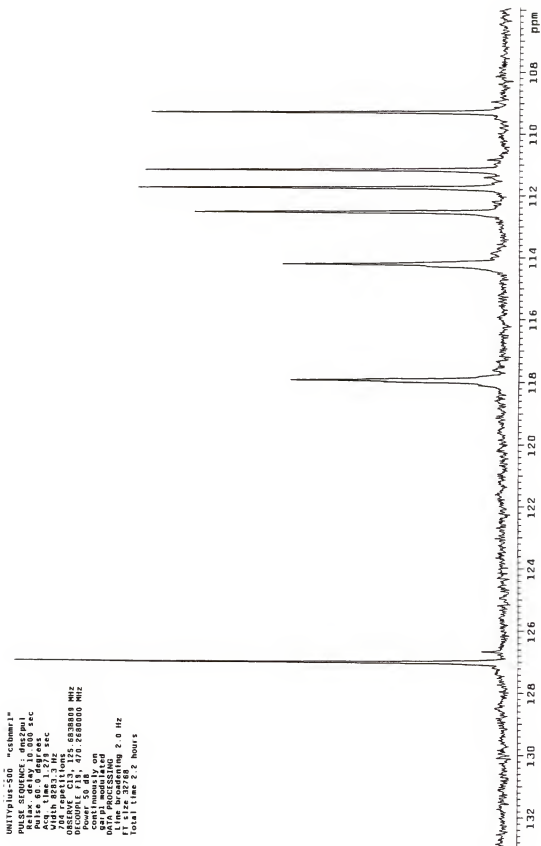
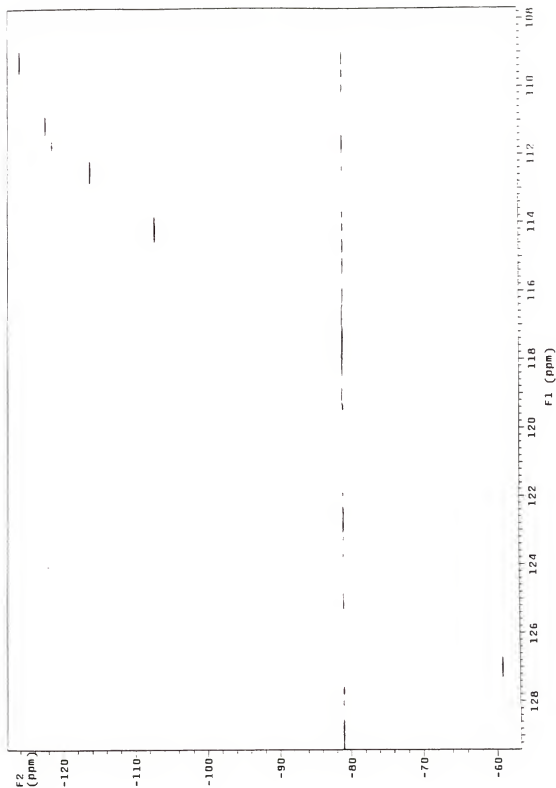


Figure 3-7. HMQC Spectrum of Compound V
1,2,2-Trichloroperfluorooctane

1,2,3-Trichloroparf luoro-octene
125-MHz
Heteronuclear Multiple Quantum Coherence



each a triplet of pentets respectively located at 111.2, 111.8, and 112.5 ppm. Peak *c* is a triplet of triplets located at 114.3 ppm, and we find the multiplet *g* at 109.1 ppm. The one-bond coupling constants for carbons *c* through *g* are found in the small range of 275.5 ppm and 270.0 Hz. The two-bond coupling constant for these atoms are found inside the a small range of 33.3 and 31.3 Hz. Table 3-2 summarizes the peak assignments and the corresponding nuclear coupling.

Table 3-2

<i>Carbon Nucleus</i>	<i>Chem. Shift (ppm)</i>	$^1J_{CF}$ (Hz)	$^2J_{CF}$ (Hz)	$^2J_{CF}$ (Hz)
<i>a</i>	127.0	301.7		4.1
<i>b</i>	117.9	287.9	33.1	4.7
<i>c</i>	114.3	275.5	31.3	3.8
<i>d</i>	112.5	274.6	31.4	
<i>e</i>				
<i>f</i>	111.2	271.3	32.3	
<i>g</i>	109.1	270.4	33.1	
<i>h</i>	85.2			

2,2-Dichloroperfluorodecane (VI). The carbon-13 spectrum for dichloroperfluorodecane is shown in Figure 3-8. It resembles the spectrum in Figure 3-5 in its general appearance. The number 1 carbon atom in the chain yields an intense quartet centered at 121.5 ppm, and the 284.8 Hz one bond coupling constant for this quartet, labeled *a*, is easily measured. The tenth carbon atom in the chain yields a quartet of triplets, *b*, at 118.1 ppm. The one-bond coupling is 287.6 Hz and the two-bond coupling is 33 Hz. We assign the sextet at 81.9 ppm to the number 2 carbon atom bearing the two chlorine substituents. The splitting in this resonance is 37.7 Hz.

The rest of the spectrum is composed of overlapping triplets of multiplets from the difluoromethylene groups. The bilevel decoupling experiment is shown in Figure 3-9, and

it does not indicate any residual coupling over the 25 kHz fluorine spectral width, but we require the heteronuclear correlation experiment to assign the remaining peaks.

Figure 3-10 is the HMQC spectrum of this molecule. Like the assignments in the



VI

compound V, the carbon assignments in this molecule closely follow the fluorine chemical shift assignments, and the correlation spectrum in Figure 3-10 resembles a single curve. Peaks *c* and *d* are assigned to the third and fourth carbon atoms in the chain. Peaks *f* through *h* are respectively assigned to the seventh through ninth carbon atoms. In Figure 3-9, we observe two singlets that partially overlap near 111.9 ppm and are not resolved in the HMQC spectrum. Since they cannot be assigned unambiguously, we label carbon atoms 5 and 6 in the decane chain *e*.

Table 3-3

Carbon Nucleus	Chem. Shift (ppm)	$^1J_{CF}(\text{Hz})$	$^2J_{CF}(\text{Hz})$
<i>a</i>	121.4	284.8	
<i>b</i>	118.1	287.6	33.1
<i>c</i>	113.8	273.5	31.1
<i>d</i>	112.8	274.7	34.1
<i>e</i>	111.9		
<i>f</i>	111.8	271.4	31.7
<i>g</i>	111.2	271.4	31.7
<i>h</i>	109.8	270.8	31.7
<i>i</i>	81.9		37.7

Table 3-3 shows a summary of the peak assignments along with the corresponding one- and two-bond coupling constants. The one-bond coupling constants for the seven

Figure 3-8. Coupled Carbon-13 Spectrum of Compound VI
2,2-Dichloroperfluorodecane

2,2-Dichloroperfluordecane

Solvent: acetone
 Temp: 35
 User: 1-14-87/236.1 K
 File: C0434-1
 Multiplus-500 "csbmw1"
 NUC1: SEQUENC 15.000 sec
 Relax: 60.0 degree sec
 Acq time: 1.280 sec
 Aft: 30.000 Hz
 1536 repeats
 OBSERVE C13, 125.6824376 MHz
 DECOUPLE F19, 470.2680000 MHz
 on during delay
 off during acquisition
 spin locked
 data processed
 line broadening 2.0 Hz
 FT size 131072
 total time 6.9 hours

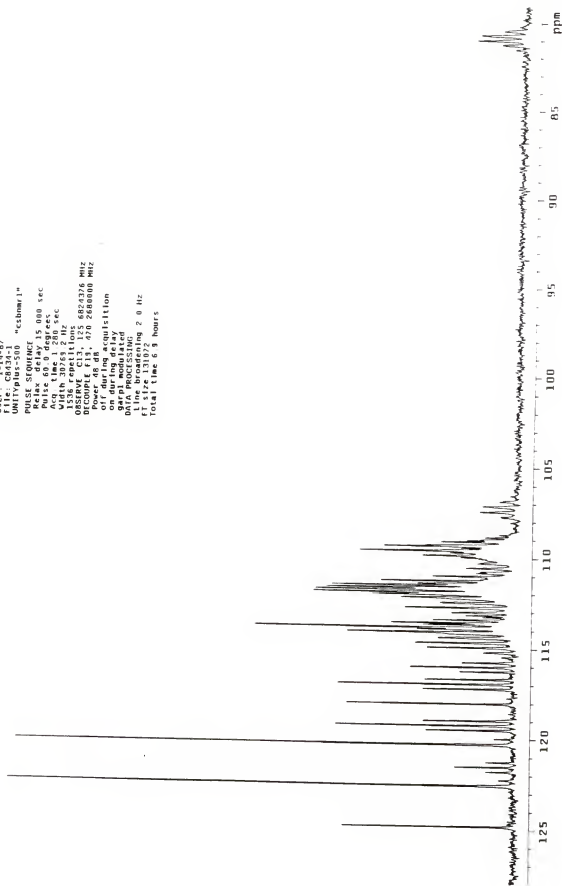
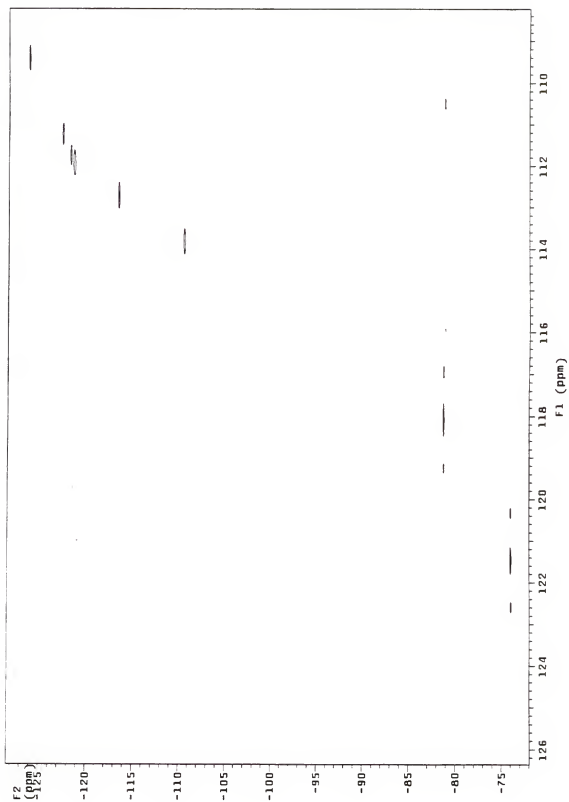


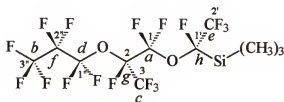
Figure 3-9. Decoupled Carbon-13 Spectrum of Compound VI
2,2-Dichloroperfluorodecane

Figure 3-10. HMQC Spectrum of Compound VI
2,2-Dichloroperfluorodecane



remaining carbon nuclei range between 275 and 271 Hz, and the range in the two-bond coupling constant is between 34 and 31 Hz.

Trimethyl[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-silane (XV). We will maintain a system of labels that corresponds closely with the fluorine assignments previously discussed in Chapter 2. The coupled carbon spectrum for compound XV is shown in Figure 3-11. Several overlapping quartets are evident between 126 and 114 ppm where we expect to find the three trifluoromethyl carbons *b*, *c*, and *e*. There are also overlapping multiplets between 111 and 102 ppm where we expect to find the chiral carbons *g* and *h*.

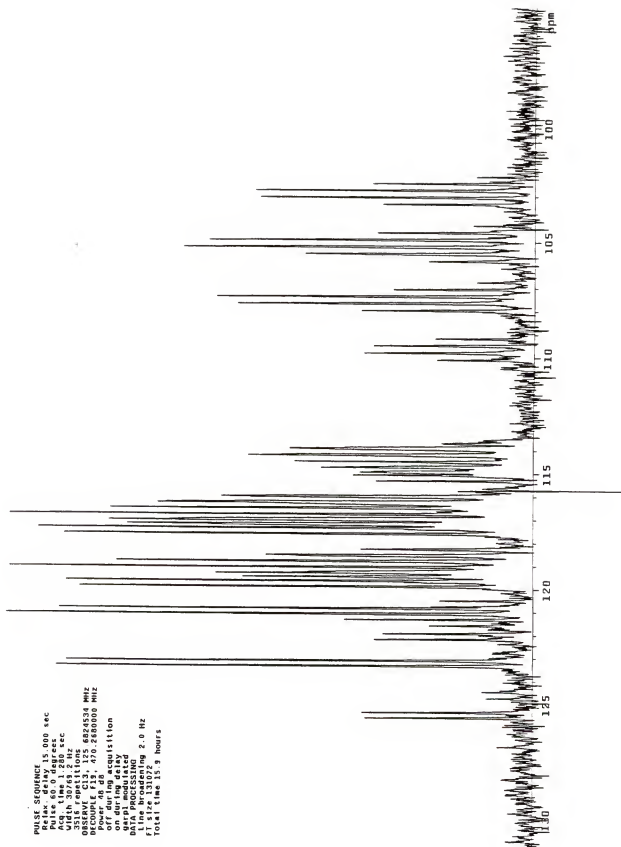


XV

Although it is fairly tedious, one can search for the expected splitting patterns by carefully measuring the distances between the individual peaks in the cluster. By doing so, it is possible to pick out a quartet of doublets centered at 122.0 ppm, another quartet of doublets centered at 118.4 ppm, and a quartet of triplets centered at 117.98 ppm. Based on its multiplicity, we can assign the quartet of triplets to the trifluoromethyl group, *b*, at position 3' attached to the difluoromethylene group. The other two quartets are further split into doublets and must therefore be close to a single fluorine nucleus, as are the trifluoromethyl groups, *c* and *e*.

The region between 118.0 and 114.0 also contains two triplets: a triplet of doublets centered at 117.2 ppm, *a*, and a triplet of triplets centered at 116.2 ppm, *d*. The fine structure in these two triplets compels us to assign *a* to the difluoromethylene carbon at position 1, and assign *d* to the CF₂ at position 1'.

Figure 3-11. Coupled Carbon-13 Spectrum of Compound XV
Trimethyl[1,2,2,2-tetrafluoro-1-[1,1,2,3,3,3-hexafluoro-2-(heptafluoropropoxy)propoxy]ethyl]-silane



PULSE SEQUENCE
 Relax delay 15.000 sec
 Pulse 60.0 degree
 Acquisition time 2.000 sec
 Width 30748.2 Hz
 3516 repetitions
 OBSERVE C13, 125.6824534 MHz
 P1 12.000 sec
 Power 48.075.2800000 MHz
 off during acquisition
 off during acquisition
 off during acquisition
 garpi modulated
 DATA PROCESSING
 Time averaging 2.0 Hz
 Line broadening 0.3 Hz
 F1 49.33602
 Total time 15.9 hours

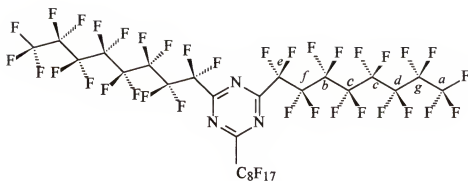
At lower frequencies we find still more overlapping resonances. We find a triplet of sextets centered at 107.6 ppm, and a doublet of pentets centered at 103.9 ppm. The triplet of pentets must be due to the remaining difluoromethylene group, *f*, at position 2". The doublet of sextets must belong to the two carbon atoms at position 2 in the backbone of the fluoroether chain, *g*. It is likely that a doublet of quartets, corresponding to the number 1' carbon in the chain, also resonates in this general area, but we do not easily recognize the quartets inside the maze of sextets found in this region. Table 3-4 summarizes the carbon-13 spectrum assignments, multiplicities, and coupling constants.

Table 3-4

Peak	$\delta\nu^{13}\text{C}$ (ppm)	description	$^1J_{\text{CF}}$	$^2J_{\text{CF}}$	assignments
<i>c</i> or <i>e</i>	122.0	quartet of doublets	285.60	30.28	O-CF(CF ₃)
<i>c</i> or <i>e</i>	118.4	quartet of doublets	287.26	31.45	O-CF(CF ₃)
<i>b</i>	118.0	quartet of triplets	286.50	32.73	CF ₃ CF ₂ CF ₂
<i>a</i>	117.2	triplet of doublets	286.50	19.56	CF(CF ₃)CF ₂ -O
<i>d</i>	116.2	triplet of triplets	287.81	31.64	CF ₃ CF ₂ CF ₂
<i>f</i>	107.6	triplet of sextets	269.42	38.51	CF ₃ CF ₂ CF ₂
<i>g</i>	103.9	doublet of sextets	269.32	37.79	O-CF(CF ₃)

Tris-2,4,6-perfluorooctyl-1,3,5-triazine (XXII).

Figure 3-12 is the carbon spectrum for this molecule. There was less of this sample available, so its spectrum displays a poorer signal-to-noise ratio than the ones shown previously. It is possible to see several overlapping triplets around 112.5 ppm, and part of *a*, a quartet of triplets centered at 118.1 ppm. Based on its multiplicity and the expected chemical shift of a trifluoromethyl group, we can assign *a* to the number eight carbon in the octane chain. However we cannot tell much more from this spectrum. In the decoupled carbon spectrum, shown in Figure 3-13, we can discern seven of the eight carbon nuclei in the sidechain of this molecule. The distorted peak at 116.0 ppm is due to a foldback from one of the solvents, hexafluorobenzene.



XXII

The heteronuclear correlation spectrum is shown in Figure 3-14. The additional dispersion in the fluorine dimension of the correlation spectrum was very helpful in assigning the spectrum of this molecule. Peak *b* is located at 112.03 ppm. In Figures 3-12 and 3-13, peak *b* is one of the overlapping carbon resonances between 112.5 and 111.0 ppm. In the HMQC spectrum, Figure 3-14, *b* is very well separated from the other carbon resonances. Like *b*, peak *c*, the resonance at 111.9 ppm, is also more clearly visible in the heteronuclear correlation spectrum than it is in Figure 3-13. The strong intensity of peak *d*, located at 111.8 ppm in Figure 3-14, suggests that this peak may represent two carbon atoms. Although peak *d* is not resolved in the correlation spectrum at 470.3 MHz, we do find this peak resolved into two overlapping peaks in the one-dimensional spectrum at this frequency.

We did not discuss the fluorine spectrum of this molecule in Chapter 2. Nevertheless the carbon assignments reflect our previously assigned fluorine one- and two-dimensional spectra at 282.3 MHz. We can easily assign the seventh carbon in the chain to the resonance labeled *g*, occurring at 109.5 ppm, because it is correlated to the fluorine peak occurring at -126.2 ppm. This is where we normally find the fluorine resonance from difluoromethylene fluorines bonded to a terminal trifluoromethyl group.

In the fluorine homonuclear correlation spectrum, we see that the peak located at -81.1 is correlated with the fluorine resonating at -122.5 ppm. These nuclei would likely be the fluorines at position 6 in the carbon chain. The nuclei at this latter location are in

Figure 3-12. Coupled Carbon-13 Spectrum of Compound XXII
2,4,6-Tris(perfluorooctyl)-1,3,5-triazine

Figure 3-13. Decoupled Carbon-13 Spectrum of Compound XXII
2,4,6-Tris(perfluorooctyl)-1,3,5-triazine

PULSE SEQUENCE: dnt2pul
 Relax delay 10.000 sec
 Acq. time 1.280 sec
 Width 30768.2 Hz
 OBSERVE F13, 475.6824337 MHz
 DECOUPLE F19, 476.2680000 MHz
 Power 56 dB on
 carrier modulated
 garpi modulated
 DATA PROCESSING
 Gain 1.000000
 FI size 131072
 Total time 3.2 hours

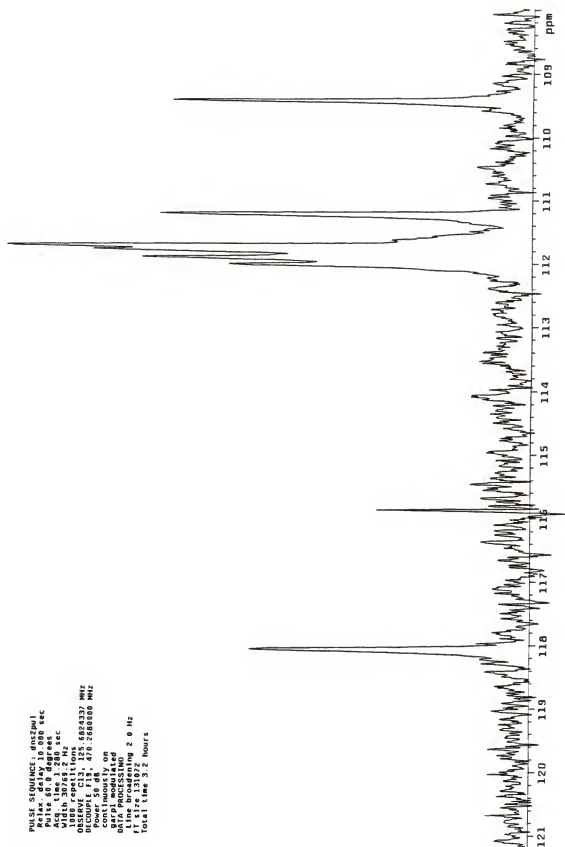
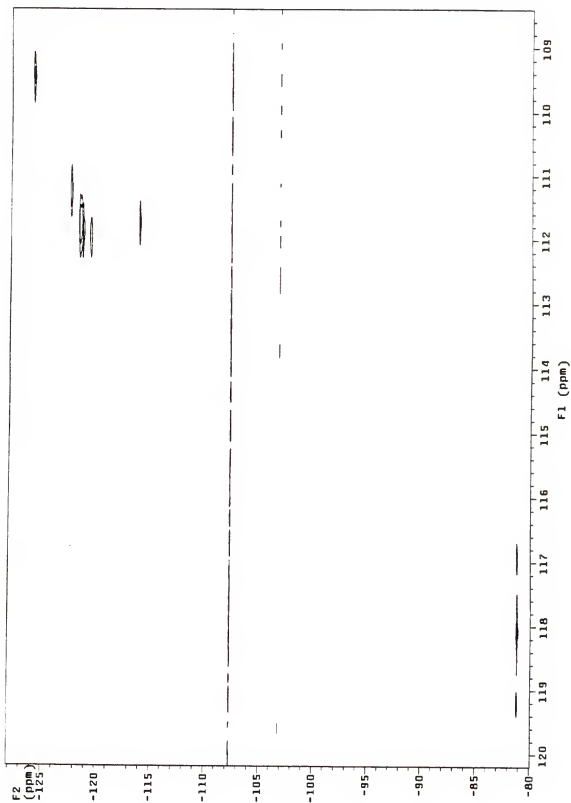


Figure 3-14. HMQC Spectrum of Compound XXII
2,4,6-Tris(perfluorooctyl)-1,3,5-triazine



turn correlated with the fluorines resonating at -122.3 ppm. As the area of the peak at this location is twice the area of the peak at -122.5 ppm, it is likely that these fluorines are associated with those at position 5 or 4. These nuclei are in turn correlated with fluorine resonating at -123.3 ppm, making this the fluorines at position 2. If we start at position 1 in the carbon chain, we see that these nuclei, resonating at -116.8 ppm, are correlated with the peak at -121.5 ppm. Thus the nuclei at this position are likely the fluorines at position 3 in the chain. These nuclei are in turn correlated with the nuclei resonating at -122.3 ppm. Thus it is likely that this peak is due to the four fluorine nuclei at positions 5 and 4.

From the heteronuclear correlation spectrum, we assign *b* to the number 3 carbon atom in the side chain based on its correlation with a fluorine resonance at -121.5 ppm. Peak *c* correlates to a fluorine resonance that we previously assigned to positions 4 and 5 in the side chain located at -122.3 ppm. Although it does not appear from Figure 3-13 that peak *c* is associated with two carbons, it is not possible to assign *c* unambiguously to one of the carbons at position 4 or 5. Peak *d* is correlated with the fluorine peak at -122.5 ppm. Therefore we assign it to the carbon atom at position 6. Likewise, *f* is assigned to the carbon atom at position number 2 because it correlates to fluorines located at -123.3 ppm that are assigned to that position in the chain. We assign peak *e* to the carbon at position 1 because it correlates with the corresponding fluorine nuclei.

The carbon assignments in the previous two chloroperfluoroalkane chains, compounds V and VI have an ordering identical to that of their fluorine assignments. Another chloroperfluoroalkane that we did not discuss in this section, compound IV, also shows this trend. However the carbon and fluorine chemical shifts in compound XXII are not related so closely. Peak *e* is located at 111.7 ppm where it overlaps peak *d* in the carbon spectrum. We assign *e* to carbon atom at position 1 because it correlates with the fluorine resonance at -116.4 ppm. So the fluorine chemical shift at this position in the side chain occurs at a relatively higher frequency than does that of the carbon nucleus to which it is directly bonded.

CHAPTER 4 CARBON-FLUORINE INDIRECT SPIN-SPIN COUPLINGS

Survey of Carbon-Fluorine Coupling Constants

Several workers have studied the carbon-fluorine nuclear spin-spin coupling for very small molecules.^{73,74} Many of these investigators followed a practice first introduced by Pople, McIver, and Ostlund⁷⁵ for calculating the coupling constant with a semi-empirical method. When evaluating the bond order matrix and the one-center integrals, the basis set functions are restricted to a fixed exponential form. As a result, the contact term becomes proportional to

$$a_{NmN'n} = \langle \phi_{Nm} | \delta(r_{KN}) | \phi_{Nm} \rangle \langle \phi_{N'n} | \delta(r_{KN'}) | \phi_{N'n} \rangle = s_{Nm}(0)^2 s_{N'n}(0)^2 \quad 4.1$$

where $s_{N'}^2(0)$ is the electron density at the nucleus of the valence s orbital on atom N' . Moreover, the non-contact terms are simplified with

$$b = \langle \phi_{Nq} | r_{KN}^{-3} | \phi_{Nq} \rangle \langle \phi_{N's} | r_{KN'}^{-3} | \phi_{N's} \rangle = \langle r^{-3} \rangle_{Nq} \langle r^{-3} \rangle_{N's} \quad 4.2$$

The term $\langle r^{-3} \rangle_{Nq}$ is the average value of r^{-3} for an electron in the q th orbital on atom N that has an azimuthal quantum number greater than zero. The values of $a_{NmN'n}$ and $b_{NqN's}$ are usually evaluated with the self-consistent field (SCF) wavefunctions. However the resulting magnitude of $J_{NN'}$ is sometimes too small, so in many INDO calculations they are taken as empirical parameters.⁷⁶

When comparing the nuclear coupling of different atoms, it is sometimes convenient to consider the reduced coupling constant, ${}^nK_{NN'}$. The relationship between the reduced coupling and the coupling constant is defined in the following equation,

$${}^nK_{NN'} = \frac{2\pi {}^nJ_{NN'}}{\gamma_N \gamma_{N'} \hbar} \quad 4.3$$

In using the reduced coupling constant, we remove the effects of the product of magnetogyric ratios that could determine the absolute sign ${}^nJ_{NN'}$. Consider the carbon one-bond reduced coupling constant, ${}^1K_{CN'}$, as one goes across the second period from lithium to fluorine. ${}^1K_{CN'}$ increases to a maximum for $N' = \text{CH}_3$, and then rapidly decreases and becomes negative for $N' = \text{OH}$ and $N' = {}^{19}\text{F}$. Moreover, there is a substantial increase in the contributions of the non-contact terms to ${}^1K_{CN'}$ as N' increases in atomic number.

Many investigators report that the carbon one bond coupling constant depends on the s character of the bonding orbital. Muller and Pritchard⁷⁷ and later Van Alsenoy⁷⁸ presented a simple argument that takes into account only two electrons in the bonding MO that yields the relationship:

$${}^1J_{\text{CH}} \propto s \text{ character in the carbon hybrid.}$$

It also is worth noting that ${}^1J_{\text{CH}}$ correlates fairly well with the square of the bond order matrix. However, one should view this relationship with a healthy suspicion. Maciel and coworkers⁷⁴ demonstrated that a substituent effect competes fairly well with relationship between ${}^1J_{\text{CH}}$ and the bond order matrix.

In the case of ${}^1J_{\text{CF}}$, the substituent effect is found to play an even larger role.⁷⁹ Nonetheless when we do examine this trend, we see that the ${}^1J_{\text{CF}}$ becomes more

positive with increasing s character. This is compared with the trend found in carbon-hydrogen nuclear coupling, where the $^1J_{CH}$ values increase with increasing s character of the bonding orbitals of the two atoms. Both trends confirm that the Fermi contact term is an important contribution to the one bond coupling. Since the contact term is negative in the case of carbon-fluorine coupling, but positive for carbon-hydrogen coupling, the dependence of $^1J_{CF}$ on the s character of the bonding orbital is the reverse of the trend found in $^1J_{CH}$. For the most part, we may expect this opposite trend in $^1J_{CF}$ and $^1J_{CH}$ when the Fermi contact contribution is important. For example, the opposite trend in the one bond coupling is also present when one compares $^1J_{CF}$ and $^1J_{CH}$ values with ring strain. The absolute value of the one bond carbon-fluorine coupling decreases while the one bond carbon-hydrogen coupling increases with increasing ring strain.

It is reported that smaller $^1J_{CF}$ magnitudes tend to occur for the more deshielded fluorine nuclei, that is, $^1J_{CF}$ values tend to become more positive with substituents of decreasing electronegativity.⁸⁰ We extended this observation to larger and more complicated structures than were examined previously. Our results are presented in Table 4-1.

Replacing a fluorine atom with a chlorine or an oxygen atom on the carbon alpha to the CF_3 group does not change the $^1J_{CF}$ of the trifluoromethyl group, CF_3 , very much from the magnitude of 287 Hz. Substitution of a fluorine atom for a chlorine atom directly on the CF_3 group does have the appreciable effect of increasing the magnitude of $^1J_{CF}$ from 288 to 301 Hz. There is no cumulative or additive effect to $^1J_{CF}$ by substituting still another chlorine atom for a fluorine atom on the CF_2Cl group making it a $CFCl_2$ substituent.

The one bond carbon-fluorine coupling for the difluoromethylene group, CF_2 , located in the middle of a perfluorinated carbon chain does not change with the nature

Table 4-1

	<i>Molecular Fragment</i>	<i>Carbon-Fluorine Coupling</i>	
		$^1J_{CF}$	$^2J_{CF}$
1	CF ₃ CF ₂ -	287.8	33.0
2	CF ₃ CCl ₂ -	284.8	
3	CF ₂ CICCl ₂ -	301.0	
4	CFCl ₂ CF ₂ -	304.4	32.8
5	-OCF(CF ₃)-	286.4	30.9
6	-CF ₂ CF ₂ CF ₂ -	273.0	32.2
7	CF ₃ CF ₂ -	268.0	33.3
8	-CCl ₂ CF ₂ CF ₂ -	275.0	31.2
9	CCl ₂ F-CF ₂	252.6	31.7
10	-O-C(CF ₃)FCF ₂ -O	287.0	31.6
11	C ₂ H ₅ CO-C ₆ H ₄ CF ₂ -	257.0	31.6
12	CF ₃ CF ₂ CF ₂ -triazine	259.0	30.2
13	C ₆ F ₅ CFCICF ₂ CCl ₃	264.6	36.0
14	(CF ₃) ₂ CFCO-	246.3	35.5

of the alpha substituent. For example, the $^1J_{CF}$ value for the molecular moieties 6, 7, 8, and 9 is 272 Hz. However, if the difluoromethylene group is alpha to the terminal carbon in the chain, the $^1J_{CF}$ values tend to be less negative.

When the difluoromethylene group is located alpha to an aromatic ring, as they are in the molecular moieties 11 and 12, the $^1J_{CF}$ values become even more positive. We see that substituting a chlorine atom for a fluorine atom to form a fluoro-chloromethylene substituent on an aromatic ring as in the molecular moiety 13, does not extend the trend to more positive $^1J_{CF}$ values. For the methine group alpha to a carbonyl substituent in moiety 14, we report a $^1J_{CF}$ value that is substantially less

negative than the other entries. It is possible that the more positive value is a consequence of being directly bonded to ligands that are much more electropositive than fluorine atoms.

In contrast to $^1J_{CF}$ values, electronegative substituents increase $^1J_{CH}$ values from 9 to 32 Hz when the substituent is located on the alpha carbon, with halogens having the largest effect. There is no regular effect on $^1J_{CH}$ when an electronegative substituent is located beta to the carbon atom in question. However, $^1J_{CH}$ values increase when there is more than one electronegative substituents on the beta carbon.

While it is possible to find linear relations between the magnitude of $^1J_{CF}$ and the electronegativity of a substituent for a particular class of compound,^{81,82} the two-bond carbon-fluorine coupling constant, $^2J_{CF}$, is fairly invariant to the nature of the substituent. The $^2J_{CF}$ values reported in the table above average 33 +/- 3 Hz. The larger values of 36 Hz are associated with the chloro-fluoromethylene moiety 13 and the fluoromethine moiety 14. These molecular moieties are directly bonded to ligands less electronegative than fluorine. Smaller values around 16 - 20 Hz are found in fluorinated aromatic compounds.

The carbon-hydrogen two-bond coupling constant, $^2J_{CH}$, on the other hand, is negative and rarely larger than 20 Hz in absolute magnitude. The two bond carbon-hydrogen coupling constant in vinyl groups is strongly dependent on the relative orientation of the terminal carbon and hydrogen atoms⁸³ where $^2J_{CH}$ follows a sine squared dependence. A strong stereochemical dependence is demonstrated in the $^2J_{CF}$ values for haloethylenes,⁸⁰ perhaps for the very same reasons.

While the sign of the carbon-proton coupling constant tends to alternate with an increasing number of bonds separating the nuclei, the sign of $^3J_{CF}$ is reported to vary,⁷⁹ The relative sign for longer range carbon-fluorine coupling constants has not been determined. Polar substituents contribute to the magnitude of the three-bond

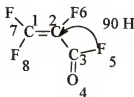
carbon-hydrogen coupling constant and, through parallel reasoning, we might expect an electronegative substituent to affect the magnitude of $^3J_{CF}$.

Grutzner et al. suggest that both $^3J_{CF}$ and $^4J_{CF}$ are conformationally dependent. Wray⁸⁴ applied the SCPT-INDO method to the problem of calculating the angular dependence of three- and four-bond carbon-fluorine couplings. His calculations also included the noncontact terms. Wray predicted $^3J_{CF}$ to be positive and dominated by the Fermi contact term. He reports the magnitude of $^3J_{CF}$ to show a dependence on the CCCF dihedral angle similar to that found for $^3J_{HH}$ and $^3J_{HF}$. A number of authors reviewing this area have indicated that subtle changes in conformation and electronic structure result in marked changes in $^3J_{CN}$ (where N' represent a first period element) as one moves across the second period.^{76,79,80} So perhaps there exist factors, other than the dihedral angle, that are important, making the angular dependence of $^3J_{CN}$ difficult to describe.

Three bond carbon-fluorine coupling constants of perfluorinated organic compounds are difficult to measure. Direct observation in the carbon spectrum is obscured by the vast multiplicities from the carbon-fluorine one-bond and two-bond couplings. Their cumulative effects also tend to broaden the resonance peaks because of unresolved overlapping splittings. Moreover, the long range indirect detection experiments often lack the resolution needed to detect $^3J_{CF}$. We measured the three-bond carbon-fluorine couplings in the fluorobenzene ring of 1-fluorophenyl-1-chloro-2,2-difluoro-3,3,3-trichloro-propane, number 13 in the table above. The average $^3J_{CF}$ value for the aromatic carbon-fluorine is 4.2 Hz, though it is not uncommon to see reported values of 10-25 Hz.

Unusual Two-Bond Carbon-Fluorine Spin-Spin Coupling

Although the average two-bond carbon-fluorine coupling constant is around 30 Hz, some carbon-fluorine two-bond coupling constants much larger than the average have been observed. Often, the nuclei exhibiting these large coupling constants are located near unsaturated moieties: acyl fluorides and/or carbon-carbon double bonds. An example molecule is propenoyl fluoride.



The spectrum of the neat propenoyl fluoride sample was recorded in this laboratory at 25 MHz on a Varian XL100. The two-bond coupling constant between the fluorine nucleus number 5 and the carbon nucleus number 2 is 90 Hz. Determining why $^2J_{CF}$ is three times larger than the norm encouraged an investigation into the orbital mechanism for transmitting the coupling constant. The possibility exists for a “through space” interaction between the nonbonding orbitals on fluorine 5 and the unsaturated moiety at carbon 2. There is also a question regarding the role of the carbonyl group in transmitting the coupling information.

We optimized the molecular geometry for this compound using the *ab initio* program GAMES, General Atomic and Molecular Electronic Structure System.⁸⁵ These coordinates were given to a group of Argentinean theorists, collaborating in this inquiry, who had developed a program designed to calculate the different contributions to the isotropic nuclear coupling constant, CLOPPA.⁸⁶

Contributions from Local Orbitals Using the Polarization Propagator Approach

The Contributions from Local Orbitals Using the Polarization Propagator Approach (CLOPPA) was used to calculate the coupling constant so that we could learn the origin of the anomalous behavior for $^2J_{\text{CF}}(\text{C}_2\text{-F}_5)$ in propenoyl fluoride. CLOPPA is an extension of the earlier Inner Projections of the Polarization Propagator (IPPP) method.⁸⁷ The polarization propagator⁸⁸ (PP) expresses the efficiency in which the various local pathways transmit spin coupling information and, thus enables us to discern the contributions from different molecular fragments to the total coupling constant. Other methods for dividing the calculated spin-spin coupling constant into components determined from the electronic mechanism involved in the perturbation include the Partially Restricted Molecular Orbitals method (PRMO),⁸⁹ and the Neglect of Nonbonded Interactions Method (NNBI).⁹⁰

In the CLOPPA method, the coupling between the two nuclei is decomposed into contributions from different molecular fragments. The fragments are sums of individual terms involving the projected polarization propagators and perturbators that define the coupling pathways.

$$J_{NN'}^A(\text{local}) = k \sum_{ia,jb} U_{ia,N}^A P_{ia,jb} U_{jb,N'}^A = \sum_{ia,jb} J_{ia,jb}^{\text{FC}} + J_{ia,jb}^{\text{SO}} + J_{ia,jb}^{\text{SD}} \quad 4.4$$

In the equation defining $J_{NN'}$, $P_{ia,jb}$ is the ia,jb element of the inner-projected polarization propagator (PP) matrix. The Fermi contact, spin-orbit, and spin-dipolar perturbators are represented by U^A . Terms such as the product of magnetogyric ratios are collected in the constant k . Each term in the summation, depends on two occupied-- i,j --and two vacant-- a,b --localized molecular orbitals (LMOs) that are chosen to represent chemical functions such as bonds, antibonding orbitals, or lone pairs. The sum runs over the LMO's that span the molecular fragment of interest.

The ground state wave function is first evaluated at the INDO level of approximation. Engelmann's projection and rotation technique, an adaptation of Verwoerd's localization method,⁹¹ is then performed separately on both the occupied and virtual molecular orbitals. The independent transformations on the occupied and vacant orbitals ensure that no virtual states are mixed into the ground state wavefunction. The subspace defined by these unitary transformations was used to build the projector, **R**. The resulting localized molecular orbitals are linear combinations of the MOs, and eigenvectors of the operator that have a maximum projection on the set of atomic orbitals.

We expect these LMOs to represent the electronic density of the molecular fragment because the occupied LMOs maximize a local density operator,

$$\rho_{local} = \sum_{\mu\nu, local} \langle \mu | \rho | \nu \rangle \langle \nu |. \quad 4.5$$

In this equation, $\langle \mu |$ and $| \nu \rangle$ are local atomic orbitals, and ρ is the electron density operator. If chemically intuitive functions are not produced at first, the LMOs are relocalized within the local fragment producing a smaller subset of orbitals. This procedure is repeated as many times as necessary. If all the MOs that have been subjected to relocalization are used, the projection subspace that defines **R** is not changed at all since only linear combinations of the original LMOs are obtained with the relocalization procedure. Although the same subspace is used, the elements of $P_{ia,jb}$ and $U_{ia,N}$ will be more easily interpreted as chemical bonds, lone pairs, and antibonding orbitals.

The projector is used to inner-project the polarization propagator on the desired subsystem, thus obtaining the matrix $P_{ia,jb}$:

$$\mathbf{P} = \mathbf{R} \left\{ \mathbf{R} \left({}^3\mathbf{A} \pm {}^3\mathbf{B} \right) \mathbf{R} + \alpha(1 - \mathbf{R}) \right\}^{-1} \mathbf{R}. \quad 4.6$$

The polarization propagator is evaluated at the random phase approximation (RPA)⁴ and ${}^3\mathbf{A} \pm {}^3\mathbf{B}$ is the triplet RPA-PP matrix whose elements ${}^3\mathbf{A}$ and ${}^3\mathbf{B}$ can be obtained from the molecular orbitals.⁹² The total contributions to the coupling constant calculated with the IPPP formalism are equivalent to those results obtained using the FPT and SCPT schemes, provided that the same ground state wave function is used in all cases.⁹³ The nonzero constant α is not critical to the evaluation of the propagator matrix $\mathbf{P}$.⁹⁴

The local contributions to the different terms of the coupling constant are determined by combining the inner-projected polarization propagator matrix elements $\mathbf{P}_{ia,jb}$ with the particular perturbator and summing over the occupied and vacant LMOs. When the perturbator is the contact term, the sum takes on the form shown below.

$$J^{FC} = -\frac{4}{h} \left(\frac{4\pi\beta\hbar}{3} \right)^2 \frac{\gamma_N \gamma_N}{3} \sum_{ia,jb} U_{ia,N}^{FC} {}^3P_{ia,jb} U_{jb,N}^{FC} \quad 4.7$$

The Fermi contact perturbator is expressed as

$${}^{FC}_{ia,N} = \langle i | \delta(r_N) | a \rangle \quad 4.8$$

The elements of $U_{ia,N}^{FC}$ form a column vector whose length is the product of n and r , where n is the number of local occupied molecular orbitals, and r is the number of local virtual orbitals. The evaluated triplet RPA-PP matrix is expressed in the following form

$${}^3P^{-1}_{ia,jb} = (\epsilon_a - \epsilon_i) \delta_{ab} \delta_{ij} - \langle ab | ji \rangle - \langle aj | bi \rangle. \quad 4.9$$

The elements of P_{iajb} form an $nr \times nr$ matrix.

The spin-orbit term requires a singlet RPA matrix that is written as

$${}^1P^{-1})_{ia,jb} = (\epsilon_a - \epsilon_i) \delta_{ab} \delta_{ij} - \langle ab | j i \rangle + \langle aj | bi \rangle, \quad 4.10$$

and the spin-orbit perturbator is expressed below

$${}^{SO,\alpha}_{ia,N} = \langle i | \frac{L_N^\alpha}{i\hbar r_N^3} | a \rangle. \quad 4.11$$

The α component of the angular momentum operator for nucleus N is represented by the operator L_N^α . The LMOs $\langle i |$ and $| a \rangle$ must have contributions from p atomic orbitals. If only p orbitals are considered, then we may picture the operator L_N^α as exciting an electron in a given p orbital orthogonal to the α axis into another p orbital orthogonal to both the original p orbital and the α axis in question.

$$\langle p_y | L^x | p_z \rangle = \langle p_z | L^y | p_x \rangle = \langle p_x | L^z | p_y \rangle = i\hbar \quad 4.12$$

The perturbator for the spin-dipolar term has the following form:

$$U_{ia,N}^{\alpha\alpha} = \langle i | \frac{3n_{\alpha\alpha}n_{N\beta} - \delta_{\alpha\beta}}{r_N^3} | a \rangle \quad 4.13$$

where $n = r_{Nz}/r_N$. This term does not provide us with a simple geometric picture, but the nondiagonal terms represent excitations that contribute when the $\langle i |$ and $| a \rangle$ molecular orbitals are composed of p orbitals that are mirror images in a plane bisecting the alpha and beta axes. The diagonal components may be interpreted as

intensifying the contribution of p orbitals lying on the axis: they generate excitations from a p orbital in $\langle i |$ to the same orbital in $| a \rangle$. This is a very different from the behavior of the nondiagonal terms and is also different from the behavior of the SO perturbators.

For propenoyl fluoride, the calculated results for the total couplings are presented in the Table 4-2 below.

Table 4-2

$N-N'$	$FC(Hz)$	$SO(Hz)$	$SD(Hz)$	$Exp(Hz)$
5-2	72.50	-0.95	0.16	90.0
6-3	1.16	-1.77	0.98	
7-2	-4.49	-7.21	5.83	
8-2	-12.41	-15.67	5.27	

CLOPPA was used to analyze the coupling pathways in propenoyl fluoride.

After the orbitals were localized, the smallest subspaces of orbitals that reproduce the total couplings are:

Occupied	Virtual
1: Bond (C2-C3)	1*: Anti-Bond (C2-C3)*
2: XY-Lone Pair on (O4)	
3: Sigma Bond (C3-F5)	3*: Anti-Bond (C3-F5)
4: Lone Pair on (F5)	

To understand the effects of the carboxy group, the coupling constant for the isoelectronic compound, 1,1,2,3-tetrafluoro-1,3-butadiene, was calculated. To our knowledge, the coupling constant for this compound has never been measured. The results are presented below:

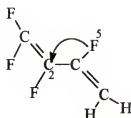


Table 4- 3

N-N'	FC(Hz)	SO(Hz)	SD(Hz)
5-2	11.26	-2.07	0.15

It is particularly enlightening to compare the effects of the following pathways in these two molecules:

1. $^2J_{CF}(C_2-F_5)$ in propenoyl fluoride where the carbonyl is the intermediate group.
2. $^2J_{CF}(C_2-F_7)$ in propenoyl fluoride where C-F is the intermediate group.
3. $^2J_{CH}(C_2-F_5)$ in 1,1,2,3-tetrafluoro-1,3-butadiene, where the vinyl group is intermediate.

The comparison reveals the relative importance of the lone pair electrons on the oxygen as compared to those located on the fluorine atom number 8, and the relative importance of the intervening pi bond as opposed to the sigma bond. Table 4-4 shows the predominant coupling pathways in the three cases enumerated above.

Table 4- 4

<i>Pathway</i>	1: ${}^2J_{CF}(C_2-F_5)$	2: ${}^2J_{CF}(C_2-F_7)$	3: ${}^2J_{CF}(C_2-F_3)$
3*-3-3*-1	76.48	34.00	37.08
3*-3-3*-3	48.54	19.94	20.14
3*-3-1*-1	45.51	26.02	-0.92
3*-3-1*-3	13.80	12.51	6.69
3*-3-3*-2	12.47	1.39	2.22
3*-4-3*-3	-35.58	-15.30	-16.97
3*-4-3*-1	-28.04	-17.66	-14.60
3*-4-1*-1	-20.06	-19.62	10.59
3*-4-1*-3	-15.50	-15.73	-8.36
1*-3-1*-1	-13.39	-10.69	-7.62
3*-4-3*-4	-9.37	-8.45	-3.70
Total Sum	74.56	6.41	24.55
Total Coupling	71.59	6.36	24.06

Inner projections can be used to exclude the influence of a lone pair orbital on the oxygen atom. If LMO number 2 is excluded from the subspace, the coupling constant is changed in the manner shown in Table 4-5.

Table 4- 5

1: ${}^2J_{CF}(C_2-F_5)$	2: ${}^2J_{CF}(C_2-F_7)$	3: ${}^2J_{CF}(C_2-F_3)$
32.05 Hz	-1.35 Hz	13.57 Hz

Excluding the carboxy oxygen lone pair results in a coupling constant of normal magnitude. Thus, it the lone pair on the oxygen atom which is vital to transmitting the large coupling constant. The coupling information is transmitted via

direct excitations from the bonding to the vacant orbitals, and it is transmitted indirectly by way of a configuration interaction expressed through the polarization propagator. We can divide propenoyl fluoride into two subspaces to discern the relative importance of the direct and indirect pathways.

The subspace designated S1 contains all the occupied (1,2,3,4) and virtual (1* and 3*) LMOs described above. The subspace designated S2 does not include the lone pair orbital 2. The total coupling is written as

$$J(S1) = J(S2) + JI(S2) + JD(S1) \quad 4.14$$

The subspace J(S2) is the coupling when inner projections are used to completely exclude LMO 2. Subspace JI(S1) is the difference in the coupling when the LMO 2 is included in the polarization propagator and J(S2), but not including the direct terms. The final subspace, JD(S1), contains only those paths that include LMO 2, and we designate as the direct contribution. Table 4-6 illustrates the different contributions:

Table 4- 6

	${}^2J(\text{C2-F5}) \text{ Hz}$	${}^2J(\text{C2-F7}) \text{ Hz}$
J(S2)	32.05	-1.35
JI(S2)	31.14	7.71
JD(S1)	8.40	~0.0
J(S1)	71.59	6.36

Hence we see that the indirect effect of LMO 18 increases the absolute value of all the coupling pathways. Moreover, there is no direct contribution of the LMO

number 18 in $^2J(\text{C2-F7})$, indicating that the lone pair on the fluorine atom number 8 does not extend out into its surrounding as does the lone pair electrons on the carboxy oxygen.

CHAPTER 5

SUMMMARY AND CONCLUSIONS

The fluorine and carbon NMR spectra of twenty-two highly fluorinated molecules were systematically studied. The following statements are concluding remarks.

- Additivity rules describe the chemical shifts of chlorofluoroalkanes and aid in assigning the fluorine resonances.
- Vicinal coupling can occur but five-bond fluorine-fluorine coupling constants are more common.
- Opposite signs were observed between a three- and four-bond coupling constant in 1,1-dichloroperfluorooctane, but a four- and five-bond coupling constant in 2,2-dichloroperfluorodecane had the same sign.
- The chemical shift difference between inequivalent geminal fluorines beta to a chiral carbon is larger than the corresponding difference between geminal fluorines alpha to a chiral carbon. Inequivalent geminal fluorines gamma to a chiral carbon have the smallest difference in their chemical shifts.
- There is no trend between the fluorine-fluorine two-bond coupling constant, $^2J_{FF}$, and their proximity to chlorine substituents.
- The carbon-fluorine two-bond coupling constant also has little correlation to substituent effects, but the carbon-fluorine one-bond coupling constant is very sensitive to the substituent effects.
- The two-bond carbon-fluorine coupling is larger than the three-bond carbon-fluorine coupling in aromatic moities. This trend is opposite the trend found in protonated aromatic compounds.

- There is a correlation between the pattern of fluorine resonances and the corresponding carbon resonances in chlorofluoroalkanes.
- The varying intensities for the crosspeaks in the fluorine autocorrelation spectrum were interpreted as evidence for through-space indirect coupling. These different intensities were used assigning specific fluorine resonances.
- Application of the principles that we use for assigning fluorine NMR resonances can identify enantiomers in a racemic mixture.

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BIOGRAPHICAL SKETCH

John West was born in 1958 in the small town of Colón, on the Atlantic Coast of the Republic of Panama. He has three brothers and one sister. John went to parochial and public schools for elementary education, and to public junior high school in Brooklyn. In 1972, he entered Power Memorial Academy. While in junior high and high schools, John was a sports enthusiast who spent many hours playing basketball on Brooklyn's inner city playgrounds. He was a member of the Power Memorial varsity track team during his junior and senior years.

During the fall term of 1976, he entered Fisk University in Nashville, TN. He joined the laboratory of Dr. I.W. Elliott in June of 1980, and he earned a Bachelor of Arts degree in chemistry and mathematics from Fisk in 1981. Later that year, John entered Fisk's graduate school, where he continued to study organic chemistry under Dr. Elliott. He earned a Master of Arts degree in chemistry in 1983. While he was at Fisk's graduate school, the Chemistry faculty gave John full responsibility for instructing the physical chemistry laboratory course. Occasionally, he would give the lectures to the class, filling in for the professor in charge. The physical chemist at Fisk took a sabbatical for two years beginning the fall term of 1983, and Fisk offered John a position as a Lecturer in the Chemistry Department, where he taught physical and general chemistry until he entered graduate school at the University of Florida in 1986.

At Florida's graduate school, John worked as a teacher's assistant instructing general chemistry laboratories in 1986, and general chemistry recitation or discussion sessions during 1987 through 1989. He served as the president of the Black Graduate Student Organization. He represented the physical chemistry graduate students at

department faculty meetings where he observed how the faculty evaluated and hired new faculty. John actively evaluated and recruited prospective graduate students for UF Chemistry Department. He counseled and trained both graduate and undergraduate students during the normal academic year and during a summer program specifically designed to introduced minority undergraduate students to scientific research. John has shared the responsibility of maintaining up to seven different NMR superconducting instruments with his supervisors, Drs. Wallace Brey and Roy King at the Department of Chemistry, and Dr. Thomas Mareci at the Center for Structural Biology. The spectrometers ranged in field strength from 4 to 14 Tesla. His primary responsibilities were to supply these instruments with cryogenes, maintain the homogeneity of main field, instruct users in how to operate the instruments, advise users as to appropriate experiments for their respective problems, and to troubleshoot these instruments should the hardware fail.

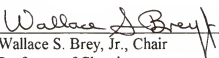
Since he joined the laboratory of Dr. Wallace S. Brey, in 1988, John has participated in several scientific endeavors involving NMR. He has studied the interaction of tightly bound and loosely bound water with monolithic silica glass with a material scientist at UF. He worked with a soil scientist in studying the interaction of hydrazine with using solid-state NMR. He studied the interactions of aluminum and acetate ions in aqueous solutions. He briefly investigated the interactions of silica and aluminum ions in mullite to understand the sol to gel process of certain glasses. John studied the tacticities of several polymers and endeavored to investigate how they bind to alumina with liquid- and solid-state NMR methods. Before General Electric made gradient-enhanced NMR spectroscopy a reality, he labored to perform this experiment.

John also worked for Dr. Richard Briggs in the Department of Radiology at the University of Florida. In Dr. Briggs' laboratory, he studied the interactions of several peptide inhibitors with the enzyme HIV Protease. John is presently employed at the Walt Disney Memorial Cancer Institute at the Florida Hospital in Orlando, Florida, where he

utilizes NMR spectroscopy to investigate molecules related to cancer therapy and blood clotting.

John married Debra D. Smith in March 1984. Though Debra is native to Nashville, John met his wife at a wedding in Alabama. Debra was guest of the bride, and John was a guest of the groom. Debra opted to attend this wedding to avoid the pain that she expected to feel upon seeing her beloved grandfather interred at his funeral. They have been together since that wedding day in Alabama.

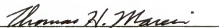
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Wallace S. Brey, Jr., Chair
Professor of Chemistry

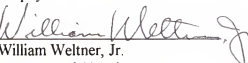
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David E. Richardson
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.


Thomas H. Mareci,
Associate Professor of Biochemistry and
Molecular Biology

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.


William Weltner, Jr.
Professor of Chemistry

I certify that I have read this study and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation for the degree of Doctor of Philosophy.


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Professor of Chemistry

This dissertation was submitted to the Graduate Faculty in the College of Liberal Arts and Sciences and to the Graduate School and was accepted as partial fulfillment of the requirements for the degree of Doctor of Philosophy.

May, 1996

Dean, Graduate School